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RABIES.

A REVIEW OF RECENT ARTICLES. XX.*

i. *Virus.*

The generalization of LEVADITI that the viruses of poliomyelitis, encephalitis, herpes, rabies and, up to a certain point, the vaccine of Jenner, form a special group which exhibit an affinity for the cellular elements derived from the ectoderm, is well known (LEVADITI, *Ectodermoses neurotropes*, Paris 1922, Masson). LEVADITI and SCHOEN[1] examine whether evidence of the presence of the virus of rabies is to be found in ectodermic structures other than nervous tissues. They have now demonstrated the presence of oxyphil formations resembling Negri bodies in the corneal epithelium, and in the Gasserian ganglion. These bodies were very abundant, and in the Gasserian ganglion were accompanied by neuronophagy. Their presence is, however, not constant.

In a very detailed paper NICOLAU, MATHIS and CONSTANTINESCO[2] discuss the characteristics of a strain of virus of *Oulou-fato*. They claim that it is less virulent, and more difficult to fix, than is the true rabies virus. The Negri bodies which the Oulou-fato virus gives rise to, differ from those of the classic rabies virus in staining blue with Mann's stain, and they are more pleomorphic. On the other hand there is a perfect cross-immunity between the classic and the Oulou-fato viruses.

REMLINGER[3] summarizes the results of his investigations during recent years on rabies in East and West Africa. He believes that the reported difficulties of fixation of African strains of virus are due to technical errors, and says that "*Oulou-fato* is an obsolete term which ought to disappear from the nomenclature."

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* For the nineteenth of this series see Vol. 30, p. 575.

[1] LEVADITI (C.) & SCHOEN (R.). Présence de formations oxyphiles ressemblant aux corps de Negri, dans l'épithélium cornéen des lapins rabiques.—*C. R. Soc. Biol.* 1933. Vol. 114. No. 31. pp. 501–504. With 2 figs.

[2] NICOLAU (S.), MATHIS (C.) & CONSTANTINESCO (Val.). La rage autochtone (maladie du chien fou) en Afrique occidentale française (étude critique et expérimentale).—*Ann. Inst. Pasteur.* 1933. June. Vol. 50. No. 6. pp. 778–839. With 26 text figs. & 16 coloured figs. on 1 double plate. [Refs. in footnotes.]

[3] REMLINGER (P.). Sur le comportement du virus rabique en A.O.F. et en A.E.F.—*Bull. Soc. Path. Exot.* 1933. July 12. Vol. 26. No. 7. pp. 941–946.

Plantureux[4] has examined the behaviour of mixtures of fixed and street virus. He finds that the Algerian strain of fixed virus (1,797th passage) when mixed with street virus retains the incubation period of the fixed virus strain, but has the infective power of street virus, when tested by intraocular inoculation. When the Tangerian strain of fixed virus, which is in approximately its 2,400th passage, is employed, the result is entirely different—when inoculated intracranially the mixture behaves like fixed virus, and when inoculated into the eye it behaves as street virus. Later experiments with mixtures containing the Algerian strain of fixed virus (then in its 1,872nd passage) yielded results which approximated more closely to those obtained with the Tangerian strain. Until the behaviour of such mixtures is more precisely defined, it seems needless to consider the suggestion of the author that certain accidents following the exhibition of fixed virus may be due to the action of mixed strains.

Remlinger and Bailly contribute a series of papers on the pseudorabies of Aujeszky. In the first[5] they state that the virus of the pseudorabies confers rabies when 0·5 cc. is injected subdurally into the rabbit, in dilutions of 1 in 500,000 (*cf.* the virus of herpes 1 in 10,000, the fixed virus of Tangiers 1 in 300,000, to 1 in 500,000). Also that the behaviour of the virus when submitted to the action of heat, and of sulphuric ether is sensibly the same as that of the virus of rabies. On the contrary the former is much more resistant to desiccation than the latter. In a second communication[6] they show that the pseudorabies virus has the same properties of diffusibility as have the viruses of rabies and of herpes. In a third paper[7] they advocate the intraocular route in experimental infections because when the fatal issue is sudden, as is usually the case in pseudorabies, there is no difficulty in being certain of the cause of death. Excoriations of the eye were almost always to be seen, and pruritus was present in 48 out of 57 cases. Thus the diagnosis is "sure and precise." The condition of the eye throughout the course of the disease is described in detail. In a fourth communication[8] they show that the virus of pseudorabies is extremely resistant to desiccation. The virus when emulsified and spread on a thin sheet on glass, did not lose infectivity in 20 days.

Further studies in pseudorabies are presented by Hurst.[9] The histology of the brain in the rabbit, the guineapig, the monkey, the

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[4] Plantureux (E.). Recherches sur le pouvoir pathogène des mélanges de virus rabiques fixes et de virus des rues. Variabilité des propriétés des virus fixes.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 26. pp. 1141–1143.

[5] Remlinger (P.) & Bailly (J.). Action de la dilution, de la chaleur et de l'éther sulfurique sur le virus de la maladie d'Aujeszky.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 23. pp. 689–691.

[6] Remlinger (P.) & Bailly (J.). Diffusibilité du virus de la maladie d'Aujeszky. —*C. R. Soc. Biol.* 1933. Vol. 113. No. 24. pp. 844–846.

[7] Remlinger (P.) & Bailly (J.). L'inoculation du virus de la maladie d'Aujeszky dans la chambre antérieure de l'oeil.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 25. pp. 1020–1023.

[8] Remlinger (P.) & Bailly (J.). Sur la résistance du virus de la maladie d'Aujeszky à la dessication.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 26. pp. 1109–1110.

[9] Hurst (E. Weston). Studies on Pseudorabies (Infectious Bulbar Paralysis, Mad Itch). I. Histology of the Diseases, with a Note on the Symptomatology.—*Jl. Experim. Med.* 1933. Oct. 1. Vol. 58. No. 4. pp. 415–433. With 3 plates. [12 refs.]

cow and the pig is described in detail. Peripheral infection is transmitted, along the nerves, possibly interstitially and by the axis cylinders. On reaching the ganglia and segments of the cord, it produces primary degeneration of nerve and glia cells. The nerve cell changes are probably responsible for the cardinal symptom of itching. Death ensues soon after the virus reaches the medulla, before visible changes have been produced. In these experiments both the Aujeszky and Iowa strains were employed.

ii. *Symptomatology.*

After describing the histories of three cases of human rabies, MATILLA[10] discusses, in a general way, some of the more interesting features of the disease.

iii. *Pathology.*

HAVENS and MAYFIELD[11] present additional evidence in favour of the view that different strains of rabies virus possess the same antigenic factors but in varying proportions (see also this *Bulletin*, Vol. 30, p. 580). The results have been obtained from neutralization of virus with heterologous serum and from agglutinin absorption tests. The differences observed were quantitative rather than qualitative. From similar experiments with 3 strains of fixed virus they find that continuous passage through the rabbit results in antigenic loss, and in a pronounced change in antigenic structure.

JONNESCO[12] has conducted a series of experiments to elucidate the question whether an immunized animal which escapes infection from a subsequent subdural dose, is refractory to further subdural inoculation. Three dogs were immunized against rabies by carbolized vaccines, and were then tested subdurally with fixed virus. One died, and the other two survived. A second inoculation with fixed virus killed one of the survivors and failed to kill the other. The remaining dog having resisted three successive subdural tests, succumbed to the fourth. The brain of this last dog was not pathogenic to dogs and rabbits, but produced rabies in guineapigs and mice without modification of incubation period.

The results of experiments to determine whether rabies virus is present in the cerebrospinal fluid have so far been irregular. KERBLER[13] has further investigated the point. He found that fluid taken from sheep during the extraction of the brain and the cutting out of the cord in every instance proved infective when inoculated into experimental animals. On the contrary when fluid was carefully drawn by occipital puncture of the subarachnoid space of sheep in the last stage of rabies, it was never infective. The latter experiment was fully controlled, and was carried out on 12 sheep. The quantity of virus

[10] MATILLA (V.). A propósito de algunos casos de rabia humana.—*Rev. San. e Hig. Pública.* 1933. Aug. Vol. 8. No. 8. pp. 166–175. [14 refs.]

[11] HAVENS (Leon C.) & MAYFIELD (Catherine R.). Antigenic Properties of Rabies Virus. III. Composition of Serologic Variants and Nature of Fixed Virus.—*Jl. Infect. Dis.* 1933. May-June. Vol. 52. No. 3. pp. 364–373.

[12] JONNESCO (Demètre). Le sort du virus rabique fixe dans le cerveau des chiens immunisés.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 27. pp. 1249–1251.

[13] KERBLER (Ferdinand). Ueber den Nachweis von Lyssavirus in der Cerebrospinalflüssigkeit.—*Ztschr. f. Hyg. u. Infektionskr.* 1933. June 15. Vol. 115. No. 2. pp. 235–240.

present must have been less than 0·0002 mgm. per 0·2 cc. He also found that the fluids had no rabicidal action. He believes that the irregularity of previous observations depended upon differences of technique.

iv. *Methods of Treatment and Statistics.*

A comparative study of the relative efficacies of various methods of treatment assessed from experiments on rabbits is reported by OKUWADA.[14] The tests were carried out on a large scale and were well controlled. The batches both of treated and untreated were of the order of 15 animals. In all 4,000 rabbits were used. The test doses were 0·1 cc. of the supernatant fluid of a fresh emulsion of fixed virus, diluted in various proportions and injected subdurally. The methods investigated were (1) dried cords, (2) dilutions, (3) heating, (4) freezing, (5) carbolic acid (incubated for 48 hours at 37°C.), (6) ether, (7) glycerin, (8) formalin, (9) gastric juice, and (10) artificial gastric juice. The experiments are set out in 8 tables, and the system followed was to compare selected pairs of methods of treatment with a control set. The results of each set are expressed as the minimum infective dose (*e.g.*, Pasteur treatment : 14 animals, minimum infective dose 1 in 50,000 = 0·1 c.c. (+), which means that a dose of 0·1 c.c. of a 1 in 50,000 dilution of the supernatant fluid of a freshly prepared emulsion of fixed virus was the lowest dose which brought about successful infection). [It would have been more convincing if the author had employed some method of recording his results which would have given information as to the regularity of the readings from which his minimum infective doses are obtained. The reviewer would suggest that the results of this huge experiment, involving enormous labour, are worthy of a much fuller presentation than he has given us. At the present the reviewer can do no more than quote the conclusions.] He finds (1) that large doses of killed virus are preferable to lesser doses of live virus as they achieve an equally high degree of immunity without incurring other risks ; (2) that yatren or ether are better than carbolic acid as killing agents, and recommends the use of a combined ether-yatren method in practice ; (3) that " nerve tissue substance itself plays no part in the antigenic equipment of the material as used for antirabic immunization. It acts as inert matter, in this respect, and may be as well done away with. The clear supernatant liquid, obtained from brain emulsion, contains a large bulk of rabies virus and it is of the same antigenic value as the emulsion from which it was prepared."

A medicament of unknown constitution, and said by the Chinese sender to be a radical cure for rabies has been tested by REMLINGER and BAILLY.[15] The tests were carried out on 4 dogs and 2 rabbits ; all succumbed after the usual incubation periods.

D'AUNOY and FINE[16] report that 372 persons were treated at New Orleans in 1931 and 230 in 1932, with Semple's vaccine. No mention

[14] OKUWADA (Masaichi). Comparative Experimental Study of Various Methods used for Antirabic Preventive Treatment. (Report I.)—*Kitasato Arch. Experim. Med.* 1933. Oct. Vol. 10. No. 4. pp. 279–297.

[15] REMLINGER (P.) & BAILLY (J.). Un prétendu médicament chinois contre la rage.—*Bull. Soc. Path. Exot.* 1933. May 10. Vol. 26. No. 5. pp. 712–714.

[16] D'AUNOY (Rigney) & FINE (Archie). Report of the Pasteur Institute of the Charity Hospital of New Orleans for the Years 1931–1932.—*New Orleans Med. & Surg. Jl.* 1933. Oct. Vol. 86. No. 4. pp. 236–238.

is made in the report of deaths from rabies or of post-vaccinal sequelae, but as the writers conclude from their experience that the method is "safe, effective and economical" it may be assumed that no untoward incidents occurred.

From the report of the Pasteur Institute at Tunis[17] for 1932, it appears that of 1,150 persons treated, 6 developed rabies, 2 during treatment, and one before the 12th day after its termination.

The statistics of the German antirabic stations for the year 1932 are summarized.[18] In all 97 persons received treatment (40 in Berlin, and 35 in Breslau), as compared with 174 in 1931. There were no deaths from rabies amongst those treated. With the exception of Breslau at which Semple's vaccine is used, the method of treatment employed was that of Högyes-Phillips. One person treated at Breslau "who had a predisposition to diseases of the central nervous system" showed symptoms of paralysis during the second week of treatment (*vide infra* No. 23).

At Calcutta[19] during the year 1931, 7,761 persons were treated; of these 43 died of rabies (0·55 per cent.). Reports regarding 67·9 per cent. of those treated were received 6 months after the termination of treatment.

v. *Rabies in Animals.*

Neitz and Thomas[20] report that during the year 1932 18 cases of rabies occurred in South Africa. Of these, 3 were in human beings, 1 in a dog, 2 in oxen, 2 in domestic cats, 3 in *Genetta felina*, 6 in *Cynictis penicillata*, and one in *Suricata suricata*. A table and a map indicate the features of these cases, and their distribution.

An epizootic of rabies is reported from Catalunya (Spain) by Roig.[21] From 1922 to 1931 the number of cases of rabies in dogs never exceeded 115 (in 1925), and in 1931 it was 67. In 1932 the number rose to 210. A strain of virus was obtained from the brain of a dog which bit 14 persons and a horse. No negri bodies were found in the brain, but the strain behaved like a strain of fixed virus when injected into experimental animals. Roig believes that it is a reinforced strain. He then goes on to discuss the prophylactic inoculation of dogs, and makes recommendations for the control of the local epizootic.

vi. *Post Vaccinal Paralyses.*

Cormack and Anderson[22] report an unusual type of post vaccinal accident occurring at Rangoon 5 or 6 days after the completion of

[17] Archives de l'Institut Pasteur de Tunis. 1933. Apr. Vol. 21. No. 3. pp. 519–537.—Fonctionnement des services de l'Institut Pasteur pendant l'année 1932.

[18] Reichs-Gesundheitsblatt. 1933. July 5. Vol. 8. No. 27. pp. 494–495. —Die Tätigkeit der deutschen Wutschutzstationen im Jahre 1932. [Compiled by Rodenbeck.]

[19] Calcutta. Eighth Annual Report of the Pasteur Institute for the Year 1931 [Nicholas (M. J.), Superintendent].—22 pp. 1933. Calcutta: Bengal Secretariat Book Depot. [Indian 8 annas: English 9d.]

[20] Neitz (W. O.) & Thomas (A. D.). Rabies in South Africa. Occurrence and Distribution of Cases during 1932.—*Onderstepoort Jl. Vet. Sci. & Animal Industry*. Pretoria. 1933. July. Vol. 1. No. 1. pp. 51–56. With 1 map.

[21] Roig I Roig (M.). Estat actual de l'epizoòtia ràbica a Catalunya.—*Rev. d. Serveis San. i Demog. Municipals de Barcelona*. 1933. Vol. 5. No. 13. pp. 24–30. With 3 figs. (1 map.)

[22] Cormack (H. S.) & Anderson (L. A. P.). Double Papilloedema following Antirabic Inoculation: Recovery.—*Indian Med. Gaz.* 1933. Aug. Vol. 68. No. 8. pp. 459–460.

treatment by Semple's method. The symptoms were those of loss of vision, complete in the case of the left eye, and partial in the case of the right. The left pupil was quite inactive to direct light and there was no consensual reaction. Ophthalmoscopic examination showed a typical papilloedema of both discs. Improvement commenced at the end of the second week, and was complete after two months. The case was considered to be a sequela of treatment for the following reasons: (1) no other cause could be discovered; (2) the incubation period conformed to that of post vaccinal paralysis; and (3) on account of the "remarkably complete recovery from such a severe condition."

A probable case of paralytic accident following treatment by Semple's method at Breslau is reported by Bock.[23] The patient had an interesting history. In 1920 he attempted to commit suicide by shooting himself in the right temporal region. This was followed by transitory blindness of the right side. In 1931 he was in hospital and amongst other symptoms had increased reflexes in the left side and ataxy of the left hand. He was a heavy drinker. At the commencement of treatment he was nervous and weak. On the 8th day he complained of headache, dizziness, and weakness of the limbs. These symptoms increased, and treatment was suspended. Thereafter followed symptoms of spastic paralysis, increased reflexes, atrophy and ataxy of the lower extremities, and paralyses of ocular muscles. The patient "is now improving." Though the cause of these symptoms might be ascribed to multiple sclerosis, or to functional disturbance, the probability that they may have had their origin in antirabic treatment cannot be excluded. The author then goes on to discuss the occurrence of such accidents in general. He draws attention to the fact that though treatment by killed vaccines reduces the risk of paralytic sequelae, it does not entirely exclude it. In other words one can no longer definitely ascribe such accidents to the presence of living virus as such. The causal factor would in his opinion appear to be an endotoxin of the virus of rabies, or a chemical constituent of the central nervous system of the rabbit. The influence of nervous predisposition would appear to be undoubted.

Patrikios and Catacouzenos[24] describe four cases of nervous complications occurring after treatment by etherized vaccines. In two the symptoms were sensory. The other two showed symptoms of paralysis. In all four albumen was in excess in the cerebrospinal fluid. These cases show that accidents may occur even when vaccines are etherized. The etiology of paralytic sequelae appears to the authors to depend upon the biotropism of a special neurotropic virus.

Getzowa, Stuart and Krikorian[25] give full details of the histopathology of the two cases of paralytic accident of the Landry type

[23] Bock (Harald). Ein Fall von wahrscheinlicher Impflähmung nach Tollwutschutzbehandlung und kritische Bemerkungen zur Frage der Impfschädigungen.—*Zent. f. Bakt.* I. Abt. Orig. 1933. July 11. Vol. 129. No. 1/2. pp. 43–50. [17 refs.]

[24] Patrikios (I.) & Catacouzenos (E.). Sur les complications nerveuses apparues au cours du traitement antirabique.—*Bull. Soc. Méd.-Chirurg. d'Athènes.* 1933. Vol. 18. No. 1. [In Greek. pp. 41–47. French summary (8 lines).]

[25] Getzowa (S.), Stuart (G.) & Krikorian (K. S.). Pathological Changes observed in Paralysis of the Landry Type: a Contribution to the Histology of Neuro-Paralytic Accidents complicating Antirabic Treatment.—*Jl. Path. & Bact.* 1933. Nov. Vol. 37. No. 3. pp. 482–500. [21 refs.] With 4 plates.

which they previously reported (this *Bulletin* Vol. 30, p. 586) and of a further case of Landry's paralysis of entirely different origin. In a review one can only give a brief summary of their findings; for further information the reader is referred to the original beautifully illustrated paper. The appearances in all these cases were similar in type. "Paralysis is due to an affection of the ganglion cells, motor and sensory alike, an affection characterised by primary nuclear changes proceeding often to complete karyolysis and final cytolysis . . . . . Between the normal ganglion-cell nucleus and its ante-mortem stage there have been encountered certain intermediate types which permit affected nuclei to be divided into three categories"—a clear basophilic type, capable of regeneration, a dark basophilic type, and a dark basophilic homogeneous type. In all three types karyolysis may occur. In addition to these fundamental ganglion cell changes, marked oedema of the grey substance, enlargement of perivascular and pericellular lymph spaces, engorgement of the small vessels, and oedema of the glia were observed. There was no evidence of focal lesions, of destruction of nervous tissue (apart from the ganglion cells), of demyelination, of change in the axis cylinders, of focal increase of neuroglia, of perivascular or pericellular aggregations, or of fat. "Such rapid involvement of the cerebrospinal axis, with nervous tissue destruction, diffuse indeed but strictly limited to ganglion cells, indicates the highly selective action of some toxin on these cellular elements of the central nervous system. The extreme activity of this toxin is best illustrated by the occasional speedy dissolution of water-clear, almost normal nuclei, while the occurrence, even if rare, of perfectly intact cell bodies, without nucleus or with a nucleus in an advanced state of degeneration, presupposes the existence of karyolysins and suggests their incrimination in a primary attack launched on the ganglion cell nuclei." They conclude that "the total absence in the central nervous system of perivascular zones of demyelination and of perivascular cuffing argues against the inclusion of antirabic treatment among the somewhat heterogeneous group of factors (small-pox, vaccinia, measles, varicella and typhoid) capable of producing acute disseminated encephalomyelitis (Westphal). It also argues against a virus theory generally." And finally, quoting from a previous paper by Stuart and Krikorian, they affirm that in so far as the causation of "accidents paralytiques" is concerned "there seems, in the basic nerve substance of all antirabic vaccines, to exist some deleterious component which, though adversely affected by various physical and chemical agencies, is still capable, in peculiarly susceptible individuals, of producing neuro-paralytic disorders."

vii. *Miscellaneous.*

Glusman, Ssolowiewa and Predteschenskaia,[26] in experiments carried out on 25 animals which had received alcohol in quantities varying from 200 cc. during 3⅛ months to 2,520 cc. during 11 months before they received antirabic treatment, observed no paralytic complications. A second experiment was carried out to check the result of Remlinger and Bailly (this *Bulletin*, Vol. 30, p. 143) that there is no evidence that alcohol has any influence upon the degree

[26] Glusman (M. P.), Ssolowiewa (J. V.) & Predteschenskaia (L. A.). Einfluss des Alkohols auf den Verlauf antirabischer Impfungen und die Ausbildung einer Immunität gegen Lyssa.—*Ztschr. f. Hyg. u. Infektionskr.* 1933. June 15. Vol. 115. No. 2. pp. 436–442. [11 refs.]

of immunity developed during treatment. The authors' experiment was carried out on 6 alcoholized and 4 control animals. The six alcoholized animals died of rabies after the usual incubation. Of the 4 control animals 2 survived. "The fact that a proportion of the control animals survived shows with certainty that in them the degree of immunity was higher than in the alcoholized rabbits." [On the assumption that the alcoholization had no effect, a result of this nature would be expected to occur about once in eight times. Hence the effect may be considered as insignificant. All the same the reviewer agrees with REMLINGER and BAILLY that "he will continue to recommend abstinence during the course of antirabic treatment, although there is no evidence that non-adherence leads to failure of treatment."]

Three rabbits were infected with *Toxoplasma caviae* and nine days later with fixed rabies virus, by NICOLAU and KOPCIOWSKA.[27] All died of rabies, with the usual symptoms. Negri bodies were found in their brains, and in addition cysts of the Toxoplasma were observed. Subpassages were made from two of the rabbits. The cysts disappeared immediately, and the concomitants of toxoplasma infection soon vanished; thereafter the passages were those of fixed virus. From a further experiment the authors conclude that previous infection with toxoplasma renders rabbits more susceptible to intra-ocular rabies infection. The practical effect of these experiments is that if accidental infection with toxoplasma occurs in the Pasteur institute, it may be rapidly eliminated by subpassage.

PLANTUREUX[28] has been unable to confirm BUSSON'S result—that variola vaccine confers an immunity against rabies (this *Bulletin*, Vol. 24, p. 231). In experiments on 24 rabbits he has observed neither delay in incubation, nor alteration in the period of sickness.

A. G. McKendrick.

[27] NICOLAU (S.) & KOPCIOWSKA (L.). Rage à virus fixe et *Toxoplasma caviae*.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 24. pp. 855–857.

[28] PLANTUREUX (R.). Rage et vaccine.—*C. R. Soc. Biol.* 1933. Vol. 113. No. 25. pp. 992–993.

MALARIA.

FEDERATED MALAY STATES. **Annual Report of the Malaria Advisory Board for the Year 1932** [KINGSBURY (A. Neave), Chairman].—16 pp. 1933. Kuala Lumpur: F.M.S. Govt. Printing Office.

Dr. R. GREEN reported to the Board on the use of atebrin. As regards the cost (see HOOPS, this *Bulletin*, Vol. 30, p. 476), seven days' treatment with atebrin should be compared with not more than seven days' treatment with quinine, because Asiatic patients will not stay in hospital longer. A course of 0·3 grams of atebrin daily for seven days, as compared with a course of 30 grains of quinine daily for the same period, would cost about £2 more for every 100 patients treated. [But, from the figures given by Dr. GREEN the usual 5-day course of atebrin would be about £2 cheaper than the 7-day course of quinine for every 100 cases.] A few patients complained of epigastric colic and supra-orbital headache after atebrin treatment. Atebrin did not act so quickly as quinine in subtertian malaria. Supplementary treatment with quinine was therefore advisable for the first 48 hours in severe cases. Like plasmoquine and stovarsol, it sometimes had a provocative effect in subtertian and might lead to an exacerbation in the first 48 hours. Atebrin seemed superior to quinine in preventing relapses. In a series of 26 benign tertian cases treated for seven days with quinine, more than half relapsed within 3 months; but in a series of 32 treated with atebrin there was only one relapse. Experiments with atebrin as a clinical prophylactic have been carried out on estates with encouraging results.

Professor K. B. WILLIAMSON invited the attention of the Board to the expense involved in the use of petrol as a larvicide for well water. He pointed out that the addition of 1 per cent. turpentine greatly increased its spreading power. The malaria carrying mosquito of the hilly country, *A. maculatus*, invaded the new hill-station of Cameron's Highlands when roads were made and the place was being developed, but Professor WILLIAMSON reported that no adult *A. maculatus* had been captured there since October 1931, "and in controlled waters only one larva of this species, and none of other anophelines, had been taken. That result had been obtained in experimental areas without the use of oil and Paris green, but by sluicing, biochemical control, and the application of white clay." Hand-worked sluice-gates were cheaply made from packing cases. the rush of water created when they were opened got rid of the larvae, These gates were more effective than the 80-gallon automatic tippers installed in some of the ravines, though the latter proved as useful as oil-spraying. Another method was the use of grass, chopped twigs, and green leaves which were piled 18 inches high and then trampled down into shallow seepage pools and drains. This method excluded light from the water, and polluted it. The results in the prevention of mosquito breeding have, so far, been very satisfactory. Masses of iron pyrites were placed at the bottom of ditches where mosquitoes were breeding and this was followed by a considerable reduction in their number, but the effect was by no means permanent. The sample used was found to contain 0·3 per cent. of arsenic.

Dr. E. A. STRUTHERS reported on successful subsoil drainage by means of short lengths of bamboo in place of earthenware pipes, a method which he recommended for inaccessible places, where transport was difficult and bamboos plentiful. *W. Fletcher.*

Lowe (G. H.). **Malaria in Rice-Fields.**—*Malayan Med. Jl.* 1933. Sept. Vol. 8. No. 3. pp. 190–192.

Anopheles hyrcanus is rarely a carrier in the Malay States, though it has been responsible for epidemics in Sumatra. The author describes three small outbreaks, in non-malarious parts of Johore, which were associated with the clearing of land for new rice fields and the subsequent prolific breeding of *A. hyrcanus*. (See Hodgkin, this *Bulletin*, Vol. 30, p. 834.) *W. F.*

Robin (L.). Recherches sur les variations saisonnières d'incidence de l'infection palustre en Indochine méridionale de 1926 à 1932. [**The Seasonal Incidence of Malaria in Southern Indochina 1926 to 1932.**]—*Bull. Soc. Path. Exot.* 1933. Oct. 11. Vol. 26. No. 8. pp. 1076–1083.

The author concludes from the records of 37,000 blood examinations made at the Pasteur Institute, Saigon, during the period 1926 to 1932, that there are two waves of malaria in the year, one of which reaches its maximum in July, and the other in December. The December increase of malaria is coincident with an increase of *A. minimus*, the principal vector, and with the maximum infection rate of this anopheline; the July wave has no apparent association of this kind, there is an increase of *A. hyrcanus sinensis* at this time, but it appears to be only an occasional vector in Cochin China. The sick rate from malaria on estates situated within the region of hyperendemicity was 59·1 per cent. in 1928, but this has fallen to 11·22 as the result of anti-malarial measures, while the rate among the general population has remained fixed at about 17 per cent. *W. F.*

Morin (Henry G. S.) & Bader (H.). Sur l'indice carbonique des eaux de surface et ses rapports pendant la mousson de N.-E avec la distribution de l'endémie palustre au Tonkin. [**The Carbonic Index of the Surface Water and its Connexion with Endemic Malaria in Tonking during the North-East Monsoon.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1933. Mar.–Apr. Vol. 11. No. 2. pp. 192–198. With 1 folding map & 1 folding chart.

It has been recognized, as the result of some 400 analyses of water from different parts of Indo-China, that an increased ratio of $\frac{CO_2}{\text{alkalinity}}$ favours the breeding of *A. minimus*, *A. maculatus* and *A. jeyporiensis*, which are the vectors of malaria in Indo-China. This index reaches very different figures in different parts of the country, and is subject to wide fluctuations with the different seasons. It is higher in the spring than in the north-east monsoon which lasts from the middle of October to the middle of April. It is very high in the deadly malarious highlands of the interior, reaching figures of 60 to 80 in some of the streams, and dropping down to 30 or less in the large rivers as they approach the plains. In the non-malarious delta of the rice-fields it falls to zero, or less, and then rises again to as much as 30 among the estuaries and river-mouths of the coast, where the water is brackish and malaria occurs. *W. F.*

Toumanoff (C.). Quelques faits nouveaux concernant le rôle de la variété tonkinoise de *A. jeyporiensis* James dans la transmission du paludisme. [*A. jeyporensis* **James a Transmitter of Malaria in Tonking.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1933. May. Vol. 11. No. 3. pp. 309–312.

The author concludes that *A. jeyporensis* James must be regarded, with *A. maculatus*, as an important auxiliary vector in regions of high endemicity in Tonking, the chief vector being *A. minimus*. This conclusion is based on the dissection of 826 specimens of *A. jeyporensis*, 6 of which he found infected, some with sporozoites.

W. F.

Kauntze (W. H.) & Symes (C. B.). **Anophelines and Malaria at Taveta.**—*Kenya Med. Dept., Records of Med. Research Lab.* No. 5. 26 pp. With 1 folding map & 2 charts.

Immunity of men, women and children of a tribe living in a hyperendemic area, but a very high infantile mortality.

The Taveta Native Reserve is situated in the low, hot plain to the south-east of Mount Kilimanjaro, at an altitude of 3,000 feet. Through it runs the Lume River, bordered by a belt of luxuriant tropical forest —damp and steamy, and full of streams. Outside the forest, is a plain covered with thorn bush. The Wataveta, who live in this reserve number between two and three thousand, but before the war, in 1913, there were 5,870 of them. In 1925 there were only 2,142, and since then, there has been only a slight increase in their numbers. Malaria is hyperendemic, and there is nearly twice as much within the forest as there is outside, half a mile from the river; but, even there, a mission station was moved four times and finally evacuated of all European staff after two missionaries had died of blackwater fever. The initial drop in the number of the Wataveta, after 1913, probably resulted from the intense disorganization of the community during the prolonged hostilities in the area. Since the war, confinement of the greater part of the tribe to the unhealthy forest, and the social conditions under which they live, have prevented all but the slightest increase in their numbers. The frequent practice of abortion is another factor; Callanan states that a girl before marriage has on an average eight to ten abortions artificially produced. The men do no work beyond making beehives. The main article of food is the banana, but there is a varied supply of foodstuffs, and the tribe is well fed. "The hyperendemic malaria . . . must necessarily have influenced birth and death rates very considerably." The infant death rate is probably about 60 per cent. The malaria vectors are *A. costalis* in the country outside the forest, and *A. costalis* and *A. funestus* within it. Cows are kept in the huts, day and night, until they become almost blind and their leg-muscles atrophy for want of use, but the mosquitoes show no inclination to neglect the human inhabitants in order to feed on the cattle.

In spite of the hyperendemicity of malaria, the Wataveta are apparently largely immune from its effects, if one excepts the high infant mortality, for one of the authors reports "the Wataveta observed by me, men, women and children, looked as healthy as any tribe I have yet seen. Certainly they complain of attacks of *homa* (fever) but these are apparently transient." *W. F.*

Senevet (G.) & Collignon (E.). Apparition précoce d'*Anopheles hispaniola* en Algérie. [**Early Appearance of** *A. hispaniola* **in Algeria.**]—*Arch. Inst. Pasteur d'Algérie.* 1933. Sept. Vol. 11. No. 3. p. 464.

In thirty years' experience Et. Sergent has never known *A. hispaniola* make its appearance before July ; it is regarded as autumnal. The authors took larvae of this species this year in April, and in May and June they became very numerous. This ante-dating of the usual appearance by three months is attributed to a warm and dry spring.

A. G. B.

Lodato (Gaspare). Le donne fezzanesi e la malaria. [**Malaria among Fezzanese Women.**]—*Arch. Ital. Sci. Med. Colon.* 1933. Nov. 1. Vol. 14. No. 11. pp. 744–748. English summary (5 lines).

Observations carried out at Fezzan (Tripolitania) in the course of an antimalaria campaign revealed the fact that in two localities specially studied, the men and children suffered severely from malaria; about 96 per cent. of the infants, 70 per cent. of the young boys and 50 per cent. of adult men, but only 7 to 9 per cent. of the women.

This enormous difference is accounted for partly by the clothing, or rather the absence of it among infants, boys and men, but more by the fact that the women are accustomed to anoint themselves with cosmetic preparations having a pungent odour, mostly that of oil of cloves, which act as repellents to anopheles. The constituents and mode of preparation of eleven of these are given. [From this it will be seen that they are more potent than the oil of citronella, the favourite local repellent in most tropical countries.] *H. H. S.*

Trinidad and Tobago. Council Paper No. 32 of 1933. **Malaria Survey for 1932.** Report of Dr. Eric de Verteuil, A.M.I.H.—27 pp. With 7 plans & graphs & 8 figs. on 4 plates. 1933. Port-of-Spain. Govt. Printing Office. [2s. 9d.]

Malaria in Trinidad is chiefly due to the breeding of *A. tarsimaculatus* in mangrove swamps and rice-fields where drainage has been obstructed. Anopheles successfully transported to London in banana storage room.

Judging from the tables in this report, malaria is severe only in certain districts. In 480 films taken at random from children and adults, the parasite rate was only 0·8 per cent., and in 306 films from school children, it was only 2·9 per cent. Within limited areas, especially in the neighbourhood of mangrove swamps where there has been interference with the natural drainage, malaria is rife. *A. tarsimaculatus*, the principal carrier, breeds most happily in water with a salinity equal to 20 to 45 per cent. of equatorial sea-water, and will breed in water containing from 1 per cent. up to 68·7 per cent. Anopheline larvae are not found in the mangrove swamps open to the sea, but where the waves have thrown up an obstructing sand-bank across an estuary or the mouth of a river, the salinity behind it is reduced, and anophelines breed there. In other places, the natural drainage has been obstructed by road or railway embankment, and swamps have formed in consequence. " In those swamps however where sea-water has been admitted and has free play daily in and

out owing to defective sluice gates, or canalization, no mosquito breeding occurs." The author recommends the installation of culverts to drain the swamps at low tide and to admit the sea at high tide, thus maintaining a salinity of 80 per cent. sea-water.

Another cause of malaria is the rice-fields, because the main drainage channels and rivers are obstructed in order to irrigate them. "The rice fields of Trinidad show as good an example of man-made malaria as could be obtained anywhere." It appears that there are "two different varieties of *tarsimaculatus* . . . *var. aquasalis* and *var. aquacoelestis*." The first breeds in brackish water, the latter breeds in sweet water. The *aquacoelestis* variety has been identified with the Brazilian species *A. oswaldoi* Peryassú.

Six batches of anopheles have been sent from Trinidad to London in Barraud's cages. The earlier batches were sent with raisins on the top of the cage for food, but many of the insects developed moulds in their stomachs and the remainder refused to feed when they arrived. Later batches were blood-fed on the day of embarkation and dispatched, in a semi-hibernating condition, in the storage room of banana boats, at a temperature of 53°F. (See Brown, below, p. 167.) The latter method was successful. *W. F.*

Missiroli (A.). Tipo epidemico delle febbri malariche si nel nord d'Italia. (**Epidemic Type of Malaria Fever in Northern Italy.**)—*Riv. di Malariologia.* 1933. July–Aug. Vol. 12. No. 4. pp. 675–688. With 4 graphs. English summary (4 lines) p. 836.

The author calls to mind Celli's three epidemic types of malaria, those of Northern Europe, North Italy and South Italy. He then describes the conditions as he finds them in Lison, Concordia and the district north of the Piave and Livenza rivers. The prevailing mosquitoes are five "races" of *A. maculipennis* (*maculipennis, labranchiae, messeae, atroparvus* and *elutus*) and the numbers caught were greatest, 9,694, in July, next 5,310 in August, 3,888 in September and 4,059 in October; thereafter they were much fewer, in November to March successively 252, 196, 28, 15 and 11. The cases of malaria recorded during the year totalled 623, of which 404 were benign tertian, 207 malignant tertian and 12 quartan. It was found that benign tertian *patients* were more numerous in April, May, and June and that the percentage of gametocyte carriers was highest in May, whereas Anopheles were most prevalent in July. Professor Missiroli observes that malignant tertian dies out at the end of spring, no cases being found among patients examined in May and June. At Portogruaro in the same locality in 1932 the highest rate of *P. vivax* schizont *carriers* occurred in September–November.

The author concludes that :—

1. The annual curve of benign tertian patients rises slightly in the spring and markedly in the summer-autumn months.

2. Malignant tertian tends to die down (esaurirsi) at the end of spring.

3. In the epidemic aestivo-autumnal period *P. vivax* is the predominant parasite, though *P. falciparum* is present also.

4. Benign tertian infections manifest themselves as a rule only in the year in which they are contracted. *H. H. S.*

WALCH (E. W.). **On the Relation between the Preference for Animal or Human Blood of Netherland-Indian Anopheles and their Ability to transmit Malaria under Natural Conditions.**—Reprinted from *Acta Brevia Neerlandica de Physiologia.* Amsterdam. 1932. Vol. 2. pp. 206–210.

Precipitin tests show that *A. ludlowi* and *A. sinensis* are not diverted from man by the presence of cattle, but that *A. maculatus* and *A. aconitus* are so diverted.

The author applied precipitin tests to anopheles caught in native houses in south Sumatra. *A. ludlowi* is the most dreaded malaria transmitter in the Dutch East Indies, and *A. sinensis* is the chief carrier in the interior of south Sumatra. As regards these two species, their preference for man was so pronounced that it made little difference whether cattle were present or not. In places where there were few cattle, 94 per cent. *A. ludlowi* and 90 per cent. *A. sinensis* contained human blood. In places where there were plenty of cattle the figures were 86 and 83 per cent. To these two androphilous species the author adds *A. leucosphyrus*, a carrier in Sumatra and eastern Borneo, *A. punctulatus*, a dangerous vector in the Moluccas, and *A. umbrosus*, an important transmitter in the interior of western Borneo. *A. maculatus*, the malaria carrier of the Malay States, fed on man when cattle were scarce—97 per cent. contained human blood—but they were diverted from man when cattle were numerous, and only 11 per cent. contained human blood. *A. aconitus* behaves similarly. Thus the presence or absence of cattle may explain why these anopheles are carriers in some places, but harmless in others. *W. F.*

CARDAMATIS (Jean P.). Relation entre les conditions météoriques et le paludisme en Grèce. (**Relations between the Meteorological Conditions and Malaria in Greece.**)—*Riv. di Malariologia.* 1933. July–Aug. Vol. 12. No. 4. pp. 689–700. English summary (8 lines) pp. 836–837.

There was a great reduction in anophelism and malaria in Greece during the year 1932; this was in part, due to the regulation of water courses and, in part, to the provision of a public water-supply which rendered the domestic storage of water unnecessary; but a similar reduction occurred in places where no sanitary improvements had been made, and the author concludes that the main cause was the exceptional dryness and heat. *W. F.*

CHRISTOPHERS (S. R.) & MISSIROLI (A.). **Report on Housing and Malaria. Being a Summary of What is Known about Anophelism in Relation to Housing and Malaria.**—*Quart. Bull. Health Organisation, League of Nations.* Geneva. 1933. Sept. Vol. 2. No. 3. pp. 355–482. With 4 figs. [17 pages of refs.]

"Screening is the one salient feature of house character which is important and effective. Next to screening in importance is the overhead fan."

Much has been added to our knowledge, especially in connexion with the differentiation of races of *A. maculipennis*, since the publication of Clayton LANE's paper on "Housing and Malaria" (this *Bulletin*, Vol. 28, p. 979.) It now appears that improved construction of houses, improved agricultural conditions, and the introduction of larger numbers of cattle are not equally effective in all areas, and

that their action in this respect is more or less limited to districts in which the anopheline carriers are certain zoophilous races of *A. maculipennis*. ROUBAUD, in 1919, concluded that cattle drew away anopheles which would otherwise have fed upon man; later, he modified this view and distinguished special zoophilous strains of *A. maculipennis* which he supposed were formed by the selective effect of habitual feeding on cattle housed under certain conditions. It is now generally recognized that the zoophilous strains are not developed in this way, but are indeed different varieties of *A. maculipennis* from those which prefer to feed on man—varieties distinguishable not only by their food-preferences, but also by differences in morphological characters, especially as regards the egg. The authors consider the term "races" as applied to the different forms of *A. maculipennis* as being ambiguous, and they regard them as "varieties" in the ordinary entomological sense; "even though the characters given in the differentiation of the adult and larva are not so definitive as might be desired, the differences in the egg appear quite reliable and sufficient." The zoophilous varieties are var. *messeae*, Falleroni, and var. *maculipennis*; these varieties are but little associated with man and, in the winter, they hibernate completely, neither laying eggs nor sucking blood. The androphilous varieties are var. *atroparvus*, van Thiel, found in Holland and Italy, and var. *labranchiae*, Falleroni, found in central and south Italy. These two varieties feed on man as well as on animals, and they do not go into complete hibernation, for though they cease to lay eggs they continue to suck blood. A synoptic table of the main morphological characters of these four varieties is given, illustrated by plates. It appears doubtful if there are similar varieties in other species, and the existence of zoophilous varieties among tropical anopheles has not been established.

"Certain regions in Europe once indisputably regions of endemic malaria have . . . become malaria-free in spite of the continued presence of anophelines. This disappearance has been ascribed in France to improved agrarian conditions leading to a more normal life of *A. maculipennis* as associated with cattle rather than man. In England, it has been ascribed to progressive improvements of a social . . . character and especially to the change in type of habitation." [See JAMES, this *Bulletin*, Vol. 27, p. 626.] The work of HACKETT, MARTINI, and MISSIROLI, however (*loc. cit.* Vol. 29, p. 832) has shown that the disappearance of malaria from certain endemic areas in Europe is largely dependent upon the absence of the malarious varieties of anopheles, namely *atroparvus* and *labranchiae*. Malaria disappears from those places in which only the zoophilous varieties, *messeae* and *maculipennis*, occur, when agrarian development, deviation from man by cattle, and other changes, such as the provision of glass windows for houses, lessen the contact between anopheles and man.

JAMES ascribed the malaria of certain houses in maculipennis countries, known as "malaria houses," to the habit acquired by mosquitoes which had lived long enough to become infected, of remaining for weeks or months in the same house, or of returning to it after every flight. It has, however, been shown that under normal conditions, especially in the tropics, anopheles remain only an extremely short time in a house, and, if they return to it, they do so only by accident and infrequently. Nevertheless, over a very large tract, including the northern parts of America, Europe and Asia, varieties of *A. maculipennis* which exhibit semihibernation continue to feed, and, as

they have ceased to lay eggs, do not leave the house during the winter. It is doubtful if the construction and character of a house in the tropics are in any way responsible for its becoming a "malaria house." This is more often due to the proximity of breeding grounds, or to reservoirs of virus in the form of native children living in neighbouring coolie lines, or to the low social and mental status of the inmates. "The 'house' cannot be considered as an isolated proposition apart from its environment . . . . Situation of a house is the first line of defence against malaria . . . . Select a situation where breeding-places within a distance of half a mile can be most readily controlled . . . . In the case of a single bungalow . . . . avoid a situation between a large aggregation of habitations and important breeding places." In many tropical countries, the neighbourhood of a native reservoir of infection is the predisposing cause of malaria and the segregation of Europeans must be considered an essential feature in the improvement of housing.

"That screening in the tropics has not been more thoroughly and systematically taken up than it has is remarkable . . . screening is the one salient feature of house character which is important, and from a preventive point of view effective." "It is doubtful how far improvements in construction, apart from the admitted value of screening would be really effective against malaria . . . Construction . . . does not . . . discourage entry of anopheles . . . Improvement in the type of house even if it had an effect in reducing malaria could scarcely be considered a reason, in a dangerous malarious area, for not completing protection by screening . . . Electrically driven fans should be provided wherever possible. . . . In all cases the essential point should be screening with the necessary free and open passage of air." By this means, mainly, it has been possible to re-colonize the notoriously malarious parts of the Pontine Marshes. "The use of electrically driven overhead fans associated with screening is an enormous advantage. . . . The use of overhead fans in screened barracks has given excellent results in India. . . . In blackwater-fever areas, it is the chief hope of combating this disease. . . . Any question whether a house by its open and well-ventilated condition is made less suitable to malaria becomes less important by the fact that, if malaria does exist, it is the proper procedure to screen the house. . . . Next to screening in importance is the overhead fan."

It does not appear likely that much could be done by improved house construction or screening for the indigenous inhabitants of malarious tropical countries who live in a state of low civilization. Many millions live in huts, yet it is extremely doubtful if improved construction, or even screening would modify the incidence of malaria without fundamental changes in the lives and habits of the people. "It must be admitted that, as yet, any relation between effective malaria prevention and improvement in housing of indigenous rural populations in many non-European countries . . . does not seem apparent to the authors." *W. F.*

RUSSELL (Paul F.). **Lectures on Malaria Prophylaxis and Mosquito Control.**—*Jl. Philippine Islands Med. Assoc.* 1933. June, July & Aug. Vol. 13. Nos. 6, 7 & 8. pp. 277–288; 339–351; 381–391. [31 refs.]

Malaria cannot be reduced by drugs. Anti-larval measures are necessary. Money is insufficient for prompt control. Work must be

continuous like road cleaning. Mosquito nets most important. Method of measuring the mesh.

These lectures are so excellent that it will be surprising if they are not collected in book form. Only a few extracts can be given here. The author states at the outset that " disconcerting though it be, there is to-day no known method for eradicating malaria in the tropics promptly, at a cost within the means of the people "; but, " given plenty of money, effective control can be accomplished, despite all handicaps, in a relatively short time. On the other hand, with plenty of time it should be possible to control malaria without spending much money, provided the will to control is present." Mosquito control gives much better results than drug control. Though quinine has saved many lives, " there are few if any records of successful malaria control by the use of drugs alone." Though quinine taken prophylactically is a practical method of maintaining the efficiency of temporary expeditions into hyperendemic areas, " it may be stated definitely that quinine as a prophylactic drug is a failure." Prompt and adequate quinine treatment of all cases would undoubtedly help in reducing the incidence of malaria in a community, but patients cannot be trusted to take it. " Even with one inspector for each individual it is doubtful if success could be achieved—such is the frailty of human nature." As regards the recommendation of the League of Nations Malaria Commission that mosquitoes in houses should be sought out and killed daily by housewives, in tropical areas " no doubt the results would be astounding *if* mosquito vectors would only stay in houses and *if* housewives and children would only spend time killing them," but in the Philippines and in many other tropical countries the mosquitoes which carry malaria do not remain in the houses in the day-time. It is unlikely that malaria can be controlled in the Philippines without anti-larval measures, but except on estates and in prosperous communities the cost is almost prohibitive. A cheap method of dealing with stream-breeders is to dam the stream, storing water behind the dam for two or three days, and then releasing it. Some of the larvae are dried up, others are washed away by the rush of the released water. By using devices such as this and automatic distributors of Paris green (see this *Bulletin*, Vol. 30, p. 864) costs may be reduced. In some places the municipality could hire a full-time labourer " to spread Paris green in the malaria-producing streams week by week for the next 25 years. This could be done as routinely as street-cleaning. . . . To succeed, it is my opinion that malaria control must be carried on by local labour under local supervision, paid by local appropriations." The widespread use of quinine, atebrin and quinoplasmine should be encouraged as an adjuvant to other methods, and the central government should supply the drugs free.

As regards educational propaganda, it is the author's opinion that this should be very largely confined to the subject of mosquito-nets. Clear information is given as to the construction and hanging of nets, and also for determining the mesh. If one examines " netting closely one sees that the holes are parallel horizontally and also diagonally, but are not side by side vertically, . . . the threads of the warp are more compactly arranged than are those of the woof, . . . one first decides which is warp and which is woof . . . with a hand lens. Then one square inch of netting is marked off and the holes along the line of the warp are counted and this count is added to

the number of holes along the woof. An easy method is to cut a hole, one square inch in size, in a piece of thin cardboard. This is then laid upon the netting so that the bottom edge is along a line of warp holes and the left-hand corner at the intersection of the horizontal warp and a diagonal woof line. The mesh is the sum of the number of holes along the bottom edge of the square and the number of holes of the diagonal. The hole at the intersection is counted twice . . . In general, it is true that cotton netting having 25 to 26 holes, as counted above, made either of what in the trade is called " 30/s " thread, or of " 40/60 " thread will exclude mosquitoes." (See this *Bulletin*, Vol. 29, p. 691.) *W. F.*

i. Cantacuzène (J.), Ottolenghi (D.), Swellengrebel (N. H.) & Pittaluga (G.). **General Observations on Malaria in Deltas.**—*Riv. di Malariologia.* 1933. Sept.–Oct. Vol. 12. No. 5. pp. 980–984.

ii. Société des Nations. Organisation d'Hygiène. Paludisme dans les Deltas.—39 pp. With 6 figs. [39 refs.] C.H./Malaria/208. Geneva. 1933. Sept. Delta du Rhin [Swellengrebel (N. H.)] pp. 1–32. Considérations générales sur le paludisme dans les Deltas [" Comité des Deltas " de la Commission du Paludisme de la Société des Nations.] pp. 33–39.

iii. Swellengrebel (N. H.). Le paludisme dans les deltas. (Etudes sur le paludisme dans le delta du Rhin.) [**The Malaria of Deltas.**] —*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1932. Dec. Vol. 5. No. 4. pp. 643–679. With 6 figs. [39 refs.]

iv. ——. **Studies on Malaria in the Rhine Delta.**—*Riv. di Malariologia.* 1933. Sept.–Oct. Vol. 12. No. 5. pp. 953–979. With 6 figs. [39 refs.]

A most interesting and illuminating survey of brackish water, *atroparvus*, malaria in Holland, and of the hypothesis of gonotrophic dissociation. The summary (of iii.) does not do it justice.

The Netherlands forms the delta of the Rhine. At the beginning of the Christian era the coast line was continuous, but, in the middle ages, there was a tremendous inundation which resulted in the formation of the Zuyder Zee. Since then, much land has been gradually recovered by the method of " polders," in which an area is enclosed by banks, and the water contained within them is collected into ditches and pumped out by windmills or electric pumps. After the great inundation, the present province of North Holland consisted of little more than a chain of dunes along the edge of the North Sea. The low land which now lies between these dunes and the salt-water Zuyder Zee is thoroughly impregnated with brackish water which percolates through the banks and fills the ditches in the polders. *Anopheles maculipennis* is widely distributed throughout Holland, but the incidence of malaria does not coincide with this distribution, for it is limited to the brackish water areas. In the province of North Holland, malaria is endemic, and, in the epidemics which occur about every 20 years, some 20 per cent. of the population becomes infected. In the adjoining province of South Holland, where the water is not brackish, there is no malaria although anopheles are numerous.

The idea that a mixing of the salt water of the sea with the fresh water of the rivers causes malaria is a very old one, both in Holland and in Italy. De Vogel found the same thing on the North coast of Java,

where malaria was similarly limited to regions of brackish water. He attributed it to the influence of the water upon the anopheles which made them more susceptible to infection with malaria parasites. Subsequently it was shown that the real cause was the presence of a special salt-water-breeding mosquito, *A. ludlowi*. Similarly VAN DER HOEVEN, who noticed that the anopheles of North Holland were smaller than those of the non-malarious areas, thought that this was due to the deleterious effect of the salt water upon the larvae, and that the feebleness and small size of the resulting adults rendered them more prone to infection, and also (because they were too feeble to puncture the thick hides of animals), more prone to feed on man. It has now been shown that this is not correct, but that, as in Java, there is one special mosquito (*Maculipennis* var. *atroparvus*) of the malarious salt water districts, and another (*Maculipennis* var. *messeae*) of the non-malarious fresh water districts. This *messeae* is probably identical with the *messeae* of Italy, but it is doubtful if *atroparvus* is the same as the Italian *labranchiae* (see VAN THIEL, this *Bulletin*, Vol. 30, p. 831). Both these varieties feed on man and animals throughout the summer, and they both prefer animals to man. They leave the house or stable after feeding, and, if one of them should happen to become infected, the chances are that its subsequent feed will be on an animal, for mosquitoes in Holland are deviated from man by enormous numbers of pigs; indeed the author thinks that if this barrier were removed, both varieties of *A. maculipennis* would transmit malaria in the summer. But, under present conditions, the malaria season in Holland occurs in the spring, before anopheles are about, and sometimes there is a minor rise in the autumn, which, as KORTEWEG has shown, foretells a large outbreak of malaria in the following spring.

Var. *messeae* of the non-malarious districts is as easily infected as var. *atroparvus*, it is no more unwilling to feed on man, and, during the summer it behaves in the same way: but, in the autumn, it goes into complete hibernation. That is to say, it neither lays eggs nor sucks blood, and there is complete "gonotrophic concordance." Var. *atroparvus*, on the contrary, does not go into complete hibernation; it retires to the shelter of a house or stable, but though it ceases to lay eggs it does not cease to suck blood. Here there is "gonotrophic dissociation," and as *atroparvus* does not leave its shelter to lay eggs, it remains in a house, feeding repeatedly for long periods, and thus it infects the inmates. These transmissions occurring in the autumn and winter produce latent infections which cause the spring malaria of Holland. When the anopheline density is abnormally high, some people have so many sporozoites inoculated into them that fever occurs within the normal incubation period instead of after several months, thus producing KORTEWEG's autumn rise which foretells more malaria in the following spring, because it is, itself, a sign of abnormal anopheline density.

The large salt-water lakes are not dangerous; but, when these are reclaimed, *atroparvus* breeds in the brackish water of the ditches within the polders. Malaria in the Rhine Delta is thus made by man. Though reclamation causes malaria in the reclaimed area it protects the hinterland from the infiltration of salt water, and thus makes it more healthy. The malaria of the province of North Holland is due to reclamation, but this same reclamation has brought about the disappearance of malaria in South Holland by the substitution of fresh water for brackish, and the consequent disappearance of *atroparvus*.

There is now " anophelism without malaria " in South Holland, because the anopheles belong to the variety *messeae*.

A scheme is in progress for protecting the new land which is being reclaimed from the Zuyder Zee, by the construction of a great dam across its mouth to keep out the sea, and the formation of a fresh-water lake in the middle, from the waters of the river Yssel.

As in Holland so in other parts of the world, deltas have been made malarious by man. In the delta of the Ganges, for example, the construction of embankments has prevented the silt-laden water from inundating the land in the western portion, and there malaria is rife. In the eastern part of the delta, the muddy water flows freely over the land, but no malaria-carrying mosquitoes breed in it until the silt has settled ; this does not occur until November, too late in the year for transmission to take place, and this eastern part of the delta is perfectly healthy (this *Bulletin*, Vol. 28, p. 573). *W. F.*

TUNISIE MÉDICALE. 1933. Nov. Vol. 27. No. 9. pp. 375–438. With 3 plates & 3 figs.—Numéro consacré au paludisme (2me partie). [9 papers.] [**Malaria Number.**]

Dr. Marcel SICART deals with the seasonal variations in the proportion of the different species of malaria parasite in the northern part of Cap Bon. *P. malariae* is commonest in the cold weather, *P. vivax* when it is a little warmer, and *P. falciparum* when it is very hot. Infection with *P. malariae* is fairly constant, but it is masked by *P. vivax* in the spring and by *P. falciparum* in the autumn. Dr. R. DUPOUX counsels his colleagues not to be afraid of giving quinine to pregnant women, because malaria is far more dangerous than the drug. Dr. C. MARINI draws attention to the infantile mortality from malaria. Dr. M. KROUCH criticises the method of prophylaxis which is based on the examination of smears taken only from those whose spleens are enlarged. Where this is done, many carriers remain undiscovered and untreated. He also comments upon the infection of infants under one year of age in 50 per cent. of whom he has found parasites ; he points out their danger as reservoirs of infection, because they are rarely examined and treated. He finds that the numerous bands of nomads who are the most poverty-stricken of the Tunisian population, are not only a public danger as regards plague and cholera, but also as regards malaria. He has found atebrin in small daily doses of 0·1 gram less efficient and more costly than quinine in doses of 0·2 gram (3 grains). Dr. A. SANTILLANA deals with malaria among children, and Dr. C. SPEZZAFUMO with the different means by which a latent infection may be made manifest. *W. F.*

FAGET (G. H.). **Malarial Fever in Narcotic Addicts : its Possible Transmission by the Hypodermic Syringe.**—*Public Health Rep.* 1933. Aug. 25. Vol. 48. No. 34. pp. 1031–1037.

There was an unusual prevalence of malaria among the narcotic addicts who were patients in the United States Marine hospital at New Orleans during the winter of 1932–33, several others died from malaria in the City, and a similar outbreak occurred at Galveston. The presence of the disease in this special class, and its occurrence during the non-malaria season made it probable that the infection was conveyed by the hypodermic syringe.

It was found on enquiry that the usual practice was to inoculate the drugs intravenously with a needle fitted on to a medicine dropper—the joint being luted with cigarette paper. The " dope " was often prepared in sufficient quantity for several persons to have their injections at the same time. When a " shot " was being given, a little blood was allowed to flow into the syringe, in order to show that the vein had been entered, and it was passed on to the next man without washing. This method of spreading malaria is of importance in the United States, where it is estimated that one person in every thousand is a drug addict. [See BIGGAM, this *Bulletin*, Vol. 27, p. 202, and EATON, below.] *W. F.*

EATON (L. McKendree) & FEINBERG (Samuel M.). **Accidental Hypodermic Transmission of Malaria in Drug Addicts.**—*Amer. Jl. Med. Sci.* 1933. Nov. Vol. 186. No. 5. pp. 679–683. With 2 figs.

In the year 1932, 35 per cent. of the malaria patients were drug addicts, and, during the first five months of 1933, 6 out of the 9 cases of malaria admitted to the Cook Hospital in Chicago were drug addicts. The method of self-administration was that described by FAGET (see above). Malaria among drug addicts maintains the same level throughout the year, whereas naturally acquired malaria occurs in waves. *W. F.*

KORTEWEG (P. C.). Waarnemingen bij kunstmatig opgewekte malaria. Verschillende stammen van *Plasmodium vivax*. [**Induced Malaria with Two Strains of** *P. vivax*.]—*Nederl. Tijdschr. v. Geneesk.* 1933. Oct. 7. Vol. 77. No. 40. pp. 4547–4570. With 6 figs. [Refs. in footnotes.] English summary.

Infections caused by a Dutch strain differed from infections caused by a Madagascar strain in the duration of incubation, type of fever, immunity reactions, response to salvarsan and number of merozoites.

Observations were made on 562 cases of induced benign tertian malaria. Some were infected by blood inoculation (" blood malaria ") and others by the bites of mosquitoes (" mosquito malaria "). Two strains of *P. vivax* were employed—strain H from Holland and strain M from Madagascar. Relapses never occurred in blood malaria, but mosquito malaria was more complicated and relapses were frequent.

The fever was higher in infections with the H strain. Patients immune to this strain were not immunized against the M strain. The number of merozoites was greater in the M strain. The M strain was more susceptible to treatment with salvarsan. In mosquito malaria, the average incubation periods were 21 days with the H strain and 12 with the M strain. Long latency occurred in 38 per cent. of the H and 7 per cent. of the M cases. The H strain produced mainly tertian fever, but, with the M strain, the fever was quotidian from the onset. *W. F.*

BOYD (Mark F.) & STRATMAN-THOMAS (Warren K.). **Studies on Benign Tertian Malaria. 3. On the Absence of a Heterologous Tolerance to** *Plasmodium vivax*.—*Amer. Jl. Hyg.* 1933. Sept. Vol. 18. No. 2. pp. 482–484.

Premunition is not heterologous.

Two patients who had been infected with the McCoy strain of benign tertian, and who had recovered spontaneously from the fever but still

had parasites in their blood, were bitten by mosquitoes infected with the Hughes strain of *P. vivax*. On the sixteenth day, in each case, the number of parasites began to rise and on the following day an attack of malaria began. "Even when appreciable numbers of *P. vivax* are present in the peripheral circulation, a patient with a latent benign tertian infection does not possess a heterologous tolerance to other strains of this parasite." *W. F.*

Boyd (Mark F.) & Stratman-Thomas (Warren K.). **Studies on Benign Tertian Malaria. 4. On the Refractoriness of Negroes to Inoculation with** *Plasmodium vivax*.—*Amer. Jl. Hyg.* 1933. Sept. Vol. 18. No. 2. pp. 485–489.

The authors have never failed to produce infection in white patients by the application of four infected mosquitoes, but among six negroes who were bitten for the purpose of inducing therapeutic malaria at the Florida State Hospital, three remained uninfected, and the attacks in the other three lasted only a few days. In a subsequent experiment two negroes were each bitten by 16 infected mosquitoes and 12 white controls were bitten by not more than one. The negroes remained free, but all the controls were infected. In a third experiment, an attempt was made to infect a negro child 5 years of age, but here again the negro remained free while the white controls contracted malaria. The authors conclude that the resistance is probably racial rather than acquired. *W. F.*

Giglioli (Giorgio). Contributo allo studio delle associazioni morbose della malaria : malaria ed ileotifo ; malaria e paratifo C. (**Contribution to the Study of Associations of Malaria with Other Diseases: Typhoid and Paratyphoid C.**)—*Riv. di Malariologia*. 1933. July–Aug. Vol. 12. No. 4. pp. 708–717. With 1 chart. [15 refs.] English summary p. 837.

The author has had much experience of malaria and enteric infections in British Guiana and this article is an interesting contribution to the fascinating subject of mixed protozoal and bacterial infections.

He begins by referring to Scott's work on coincident enteric fever and malaria in Jamaica (this *Bulletin*, Vol. 15, p. 252) where each is a severe condition separately but combined may cause but little disturbance. Dr. Giglioli's paper is based on 12,502 cases of malaria, 50 of typhoid fever and 142 of paratyphoid C in the course of nine years. In his experience typhoid and malaria together have no mutual influence inimically or otherwise, each apparently runs its course without any interaction, and malaria parasites were seen in the blood of 28·5 per cent. of his typhoid patients.

With paratyphoid C, however, there is undoubted inter-relation. Whereas usually this is a comparatively, sometimes exceedingly, mild condition, when malaria is present also, or in times of a malarial epidemic, the paratyphoid assumes great virulence resulting in death in certain cases. He quotes the figures from November 1926 to the following August, when among 78 patients with *Bact. paratyphosum C* infection there were 30 deaths and outside the hospital in the less accessible districts many died during the same period. *H. H. S.*

Schilling (Claus) & Neumann (Harry). Zur Epidemiologie der Malaria. [**Epidemiology of Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Oct. Vol. 37. No. 10. pp. 438–446. With 1 fig.

The authors consider that the method employed by Missiroli and Hackett at the two experimental malaria stations, Posada and Torpe, in Sardinia for the estimation of the amount of malaria is the best. In these places the amount of malaria was estimated not in the usual way by spleen and parasite indices of the population, but by the examination of the blood of newly-born infants, who were systematically examined from birth onwards. In Posada and Torpe it was found that practically 100 per cent. of the newly-born children became infected. In the author's opinion the spleen and parasite indices are far behind the "New-born Index" in accuracy. The latter index is of special importance in estimating the value of antimalarial measures; only when the frequency of infection in the new-born drops can one speak of the success of the campaign. *E. D. W. Greig.*

Lutrario (A.). Paralysie générale et paludisme. [**General Paralysis and Malaria.**]—*Bull. Office Internat. d'Hyg. Publique.* 1933. Oct. Vol. 25. No. 10. pp. 1769–1771.

Several studies have been made to determine if general paralysis is rare in areas where malaria is prevalent. The author gives a table from the Italian official returns of 1928, showing the deaths per 100,000 from general paralysis and from malaria in 19 areas. He points out that in those places where there are many deaths from malaria, there are few deaths from G.P.I. *W. F.*

Brown (J. Youngson). **The Care, Inspection and Transportation of Live Anopheles for Use in the Malaria Therapy of General Paralysis.**—*West African Med. Jl.* 1933. July. Vol. 7. No. 1. pp. 78–81. With 1 fig.

The induction of hibernation by cold storage before shipment of Anopheles is sometimes successful. Moulds are a danger. An instance of prophylaxis with plasmoquine. The difficulty of infecting *A. costalis* with *P. malariae.*

A. costalis was bred from larvae collected locally. The larvae were kept in a basin 18 inches in diameter over which was suspended a bell net of cotton mesh on a wire framework, with a sleeve in the side to admit the arm. The net was removed from the basin every day after the morning catch had been taken, because it was found that no adults hatched out during the day. Several batches of mosquitoes which had been sent to England from Lagos in Barraud's cages, and kept in the ship's hospital during the voyage, failed to arrive in a satisfactory condition; sometimes the cages were covered with moulds and all the mosquitoes were dead. The author considered that they might travel better in the ship's cold room in a state of hibernation. For this purpose, a batch was kept in a refrigerator at 15°C. for about a month before dispatch to England, and the results were rather better, for a few were alive on arrival. The author took 3,000 uninfected and 80 infected *A. costalis* with him when he went on leave to England. The cages were kept in the ship's thawing-out room at a temperature of about 69°F., but about a week later they were removed to the cabin

where the temperature had fallen to about this level, because some of the cages had become mouldy. By the fourteenth day, many of the insects had died, and the author heroically decided to feed on himself those which remained alive. By this means, he was able to deliver alive at Horton, 8 infected and some 700 uninfected mosquitoes. The mosquitoes, being engorged with blood, refused to feed ; consequently the infected insects were dissected and the sporozoites from their glands were inoculated into a couple of patients, both of whom developed subtertian malaria. The author took 0·06 gram of plasmoquine daily, beginning on the day before the mosquitoes fed and continuing until twelve days afterwards. He had no malaria until fourteen months later when he had been exposed to fresh infection in Nigeria. (See TRINIDAD above.)

About 20 per cent. of the malaria infections of children in Lagos are due to *P. malariae*, and *A. costalis* is the only carrier ; yet not one of 92 mosquitoes belonging to this species became infected through repeated feeding on three quartan gametocyte carriers. *W. F.*

MACDOUALL (J. C. S.) [Contributed by]. **Original Report of the Malaria Expedition to Sierra Leone in 1899.**—*West African Med. Jl.* 1933. July. Vol. 7. No. 1. pp. 85–89.

A reproduction of the original report on Freetown by ROSS, ANNETT, AUSTEN & FIELDING-OULD with remarks thereon by PROUT. It is an interesting and instructive document and shows that all the essentials of malaria prophylaxes were known 34 years ago. It seems probable that if the term " gnat-fever " employed by the authors had come into use the mosquito transmission of malaria would have had a quicker passage to general recognition. The practice of reprinting papers of this kind is to be commended. *A. G. B.*

BUROWA (L.). Das Knochenmarksbild bei der Malaria. [**Bone Marrow in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Sept. Vol. 37. No. 9. pp. 408–413.

The author investigated 26 cases of malaria, including all three types of parasite ; in some chronic cases the parasite was not found. To study the parasitological changes in the marrow he carried out sternal puncture by the method of Arinken. As a result of his investigations he reaches the following conclusions :—The parasitological picture of the marrow in malaria shows no quantitative difference from that of the peripheral blood, hence sternal puncture is not indicated as a diagnostic procedure in malaria. In pernicious malaria all stages of schizogony and formation of young gametocytes are seen in the marrow. He observed in the marrow, in various stages of development, a myeloid and mixed (normo-megalo-proerythroblastic) reaction, at times very marked, at others scarcely noticeable. The leucopenia of malaria cannot be explained by a reduction of leucocyte production, as the marrow shows a very marked myeloid reaction. Eosinophilia was often noted in the marrow and he considers it a favourable prognostic sign. *E. D. W. Greig.*

MORROW (T. L.) & WIEAND (W. G.). **Atebrine in the Treatment of Malaria. A Report of 53 Cases.**—*U. S. Nav. Med. Bull.* 1933. Oct. Vol. 31. No. 4. pp. 359–363.

Plasmoquine given with atebrin is more toxic than plasmoquine given alone.

Thirty patients with benign tertian and 23 with subtertian were given 1½ grains (0·1 gram) of atebrin three times a day for 5 days. The subtertian patients were given ⅙ grain (0·01 gram) of plasmoquine twice a day in addition. The patients were men of the United States Navy in Nicaragua. The blood smears usually became negative after 2½ days treatment and no recurrences occurred, but the dispersion of the men on leaving Nicaragua made it impossible to follow up more than 20 per cent. for as long as two months. Three cases were looked upon as failures because the symptoms persisted longer than 5 days although the parasites had disappeared, and consequently quinine was given which brought down the temperature. Skin discolouration occurred in 10 per cent.; it appeared on about the 5th day, and lasted 4 to 10 days. In four of the cases taking plasmoquine and atebrin, abdominal pain occurred which disappeared when the plasmoquine was stopped. The same thing occurred in several additional cases, not included in this series, when these two drugs were given in combination. Small doses of plasmoquine (0·01 gram, twice a day for 5 days) are not toxic when given alone. Atebrin appears to enhance the toxicity of plasmoquine. *W. F.*

Valcke (G.) & Bourguignon (G. C.). Etude thérapeutique et clinique de l'association atebrine-plasmochine dans le paludisme tropical. [**Atebrin combined with Plasmoquine in Tropical Malaria.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. Oct. 30. Vol. 13. No. 3. pp. 331–344.

Patients were alarmed by the toxic effects of atebrin-plasmoquine treatment.

The treatment was carried out on Europeans at Elizabethville where everyone suffers from subtertian malaria sooner or later, whether he takes prophylactic quinine or not. The drugs were given in the proportions recommended by the makers: 0·3 gram of atebrin and 0·03 gram plasmoquine daily for 5 days, with smaller doses for children. "A radical, immediate and lasting" cure was obtained in 29 out of 32 cases, but in 18 cases there were toxic symptoms. These were mostly mild, but in some cases there were severe abdominal pains and colic lasting a week or so. Those who had been poisoned told their friends, and towards the end of this short experiment the authors noticed a growing repugnance to treatment with these drugs among the public of Elizabethville. *W. F.*

Eckhardt (A. E.). Beitrag zur Verträglichkeit parenteraler Atebrin-Plasmochin-Behandlung bei Malaria. [**Parenteral Administration of Atebrin and Plasmoquine in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Nov. Vol. 37. No. 11. pp. 475–479.

Atebrin given intravenously and atebrin-plasmoquine intramuscularly.

The author, working in Tanganyika Territory, gave atebrin intravenously to several cases of malaria and found that it was well tolerated in doses not exceeding 0·2 gm. He considers that 0·3 gm., the dose recommended by the Malaria Commission of the League of Nations, is too high and may lead to very unpleasant symptoms. The parasitological effect and the rapid and certain clinical action of intravenous injections of atebrin, even in comatose cases, were very satisfactory. He is not able to draw final conclusions as the number of cases treated

was too small. In addition to giving atebrin intravenously he administered atebrin and plasmoquine intramuscularly. He treated 25 adults by this method. The cases were chiefly malignant tertian. He had very good results even in the most severe cases. Varying with age, the patients received from 0·1–0·3 gm. atebrin in combination with 0·01–0·03 gm. plasmoquine by intramuscular injection. Three of the patients had suffered from blackwater fever previously, and one was nine months pregnant ; in the latter the drugs had no action on the uterus or foetus. He considers that the advantage of the combined intramuscular injection is that the daily dose is given only once and is followed by rapid and certain action not inferior to that following intravenous injection. *E. D. W. Greig.*

Mayer (Martin). Ueber intravenöse Atebrinbehandlung der Malaria. [**Treatment of Malaria by Intravenous Injection of Atebrin.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Nov. Vol. 37. No. 11. pp. 479–484. With 6 figs.

Atebrin, 1 gm. dissolved in 1 cc. distilled water, was put up in ampoules ready for use. Before use 1 cc. was diluted with 3 cc. distilled water. By intravenous injection the author treated successfully and without any unpleasant symptoms 7 cases of malaria. He used up to 0·3 gm. atebrin in 9 cc. distilled water on three successive days. In comatose malarial cases it is not advisable to exceed 0·2 gm. at one injection. *E. D. W. Greig.*

Nezic (Eugen). Atebrin, das neue Antimalarikum. [**Atebrin in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Sept. Vol. 37. No. 9. pp. 423–427.

The author commenced his observations at the end of June 1932 and treated 79 cases of malaria with atebrin and plasmoquine simplex with good results. The drugs were given in the usual doses for adults and children. No serious toxic effects were noted, a few cases had the well known yellow discolouration of the skin, three of his patients complained of gastralgia. He considers that the number of cases treated is insufficient for a definite opinion on its merits but even now he can state that atebrin is the best antimalarial drug.

E. D. W. Greig.

Soesilo (R.). De beteekenis van chinine en enkele andere geneesmiddelen voor de gezondmaking van- en de individueele prophylaxis in- chronisch-endemische malariagebieden in den Oost-Indischen Archipel. [**The Importance of Quinine and Other Drugs Curatively and Prophylactically in Chronically Endemic Malarial Regions.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1933. Aug. 1. Vol. 73. No. 16. pp. 962–975.

Much that is contained in this article represents a careful assembly and critical discussion of the published facts relating to the use of quinine, plasmoquine and atebrin. They could not well be summarized. Trials made with atebrin, forming personal experience of the author, are specially interesting. Control persons received no atebrin while the test individuals were treated 24 hours or about 5 hours before mosquito infection and 4 to 6 days after with atebrin. The average weight of these volunteers was 51 kgm. and the maximum dose of atebrin given was 200 mgm. daily. Out of 21 who received

treatment with atebrin 6 succumbed to malaria whereas 10 out of 11 untreated persons contracted the disease. At present an active endeavour is being made to work out a satisfactory routine method of prophylactic administration of atebrin. *W. F. Harvey.*

James (S. P.). **Antimalarial Chemotherapeutic Tests at the Devon Mental Hospital.**—*Jl. Trop. Med. & Hyg.* 1933. Oct. 2. Vol. 36. No. 19. pp. 289–291.

Concerns the prophylactic action of atebrin.

Five patients at the Devon Mental Hospital were given prophylactic quinine, five were given a new synthetic preparation called phenoquine, five were given atebrin, and two controls were given nothing. The prophylactic doses were given about 4 hours before the patients were bitten by mosquitoes infected with the Madagascar strain of benign tertian, and they were continued for five subsequent days. The controls, the patients who were given quinine, and those who were given phenoquine all went down with malaria within a fortnight, but none of the atebrin group showed signs of the disease within the 30 days of observation. *W. F.*

i. Hecht (Gerhard). Pharmakologisches ueber Atebrin. [**Pharmacological Notes about Atebrin.**]—*Arch. f. Experim. Path. u. Pharm.* 1933. Apr. 24. Vol. 170. No. 2/3. pp. 328–338. With 2 figs. [13 refs.]

ii. Tropp (C.) & Weise (W.). Untersuchungen ueber die Ausscheidung von Atebrin durch Harn und Fäzes. [**Its Excretion in the Urine and Faeces.**]—*Ibid.* pp. 339–346. With 4 figs.

i. An account of atebrin and of its action in malaria appeared in this *Bulletin* (Vol. 29, p. 705 *et seq.*; Vol. 30, p. 198).

It is a derivative of akridin, a bright yellow powder, soluble in water. By ultra violet light it is stimulated to lively fluorescence which is visible in watery solution at 1 : 5,000,000. The effect of poisonous and tolerated doses was studied by oral and intravenous administration in rabbits and in cats. The action of the drug is described on the tissues, the blood, body temperature, circulation and respiration, gut and uterus, reticulo-endothelium. The distribution and excretion are shown in a table, whereby it is seen that in mice killed on the 5th day after an injection the fluorescence test still shows atebrin at the site of the injection, gall bladder and gut. The conclusion is that from the pharmacological standpoint atebrin is to be regarded as a substance with weak and uncharacteristic poisonous action. It causes on the one hand a local stimulation of tissue which in higher doses leads to gastro-intestinal symptoms, and on the other hand affects the central nervous sytem and especially the cerebrum which is stimulated by fatal doses. In intravenous injections it occasions short falls of blood pressure ; the heart itself is very resistant. Autonomously innervated organs respond hardly at all to atebrin. It is excreted very slowly ; even after 5–6 days traces of it may be demonstrated by the fluorescence test. The excreta contain only small quantities. Atebrin is subject to an internal circulation : a part is excreted by the liver in the bile and is reabsorbed by the bowel.

ii. One of the authors has shown at the Hamburg Tropical Institute that atebrin can be found in the urine of malarial patients three weeks after the last dose. They describe here the colorimetric methods used for its recovery from the excreta. In four cases investigated they

found in the urine 2–3 mgm. 6 days after the last 0·3 gm. dose. The excretion in the faeces was of the same order. For one patient who had received 2·1 gm. of atebrin, it is computed that in a period of 18 days 0·3 gm. was recoverable from the excreta, *i.e.*, about a seventh part. The physical and biological behaviour (in malarial birds) of the excreted substance permits of the conclusion that it is identical with atebrin.

A. G. B.

CHOPRA (R. N.) & GUPTA (B. M. Das). **Studies on the Action of Atebrin in Plasmodium Infection of Monkeys.**—*Indian Med. Gaz.* 1933. Sept. Vol. 68. No. 9. pp. 493–499.

Atebrin controls the invariably fatal infection of *M. mulatta* with *P. knowlesi*, better than quinine. It does not prevent relapses, but it easily controls them.

NAPIER and CAMPBELL (this *Bulletin*, Vol. 29, p. 700) studied a malaria parasite, *Plasmodium knowlesi*, in the blood of a Malayan monkey, *Macaca irus*. The parasite had little effect upon this monkey, but when it was injected into the common monkey of Bengal, *Macaca mulatta*, an intense infection resulted ; as many as 60 per cent. of the red cells became infected, and death, sometimes accompanied by haemoglobinuria, occurred in six or seven days. KNOWLES and Das Gupta (*loc. cit.*, p. 701) succeeded in transferring the infection from *M. mulatta* to man, and from man back again to the monkey. The present authors infected twelve *M. mulatta* by blood inoculation, and treated them with atebrin when the parasites had become numerous ; 0·025 gram were given daily for 3 or 4 days, either intravenously or intramuscularly. Two doses of 0·025 gram were usually sufficient to control the infection, and all phases of the parasite disappeared from the blood. " Intravenous injections of quinine are not effective against a heavy infection, unless they are repeated at short intervals of 3 or 4 hours, but one injection of atebrin suffices." Atebrin does not prevent recrudescences ; even after five days' treatment with large doses the parasites invariably reappeared in 10 to 15 days and they showed as great a virulence as in the primary infection, causing death in a few days. The recrudescence could, however, be more easily checked than the original attack ; usually, a single dose was followed by the disappearance of the parasites or their reduction to a chronic scanty infection. Whether they regain their virulence in course of time is not yet known. A monkey of 5 kgm. body weight can stand a dose of 0·025 to 0·05 gram of atebrin daily by the intramuscular route, or up to 0·025 gram intravenously. Two monkeys, which were given 0·05 gram intravenously died in a few hours. One monkey which was being treated with 0·05 gram intramuscularly suffered from diarrhoea which ceased when the drug was stopped. [Considerable confusion is being caused by the use of different names for the same species of monkey.] *W. F.*

ROW (R.), DALAL (N. P.) & GOLLERKERI (G. V.). **On the Effects of Quinine, Atebrin and Plasmoquin on Experimentally-Induced Malaria in the Macacus Monkey and on Some of the Pathological Changes observed.**—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 295–298. With 13 figs. on 4 plates.

Macacus monkeys infected with the simian parasite *P. knowlesi* die 3 or 4 days after the appearance of parasites, unless they receive specific

treatment while the proportion of infected corpuscles is well below 40 per cent. A dose of 2½ grains of quinine checks the infection, but a few parasites remain, and a recrudescence occurs in a few days which is fatal unless treated. Eventually, by means of repeated treatment, a state of equilibrium or of chronic infection is produced. If 0·025 gram of atebrin is given daily, the parasites disappear much more speedily and none can be seen after 2 days, but recrudescences occur about 10 days after the conclusion of treatment which are fatal unless it is begun again. Plasmoquine acts slowly, like quinine, and, even after long courses, recrudescences occur 10 days after stopping treatment. The state of equilibrium is brought about by fewer doses of quinine than of either of the other drugs. *W. F.*

Chopra (R. N.), Mukherjee (B.) & Campbell (H. G. M.). **The Pharmacological Action and Anti-Malarial Properties of Anhydrocotarnine-Resorcinol-Hydrochloride (a Derivative of Narcotine).**—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 255–260.

This derivative of narcotine has no curative action in monkey malaria.

It was stated before the Opium Commission, in 1895, that opium had antimalarial properties. Sir William Roberts "suggested that of the two abundant alkaloids of opium, morphia represented the anodyne and hypnotic properties of the drug, and narcotine was the bitter crystalline alkaloid resembling quinine and like that substance possessed tonic and antiperiodic properties." Chopra and Knowles (this *Bulletin*, Vol. 28, p. 137) found that narcotine had no action in malaria; it has been suggested, however, that some derivatives of narcotine might have an anti-malarial action. Anhydrocotarnine-resorcinol compound was prepared from narcotine, and tried in monkey malaria. It had no effect upon the parasites or the symptoms.* *W. F.*

Schwetz (J.), Baumann (H.) & Peel. Sur un essai de quininisation chez des nourrissons noirs. [**An Attempt to quininize Negro Babies.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. Oct. 30. Vol. 13. No. 3. pp. 321–329.

This attempt proved impracticable.

The authors found that 85 per cent. of the infants brought to the clinic at Stanleyville had parasites in their blood, and 50 per cent. had gametocytes. About 12 per cent. were infected with *P. vivax*, which is very rare in adults. It was difficult to get the mothers to bring the babies to the clinic regularly, but most of the infants received a small dose of "quinine" twice a week for 6 weeks. This reduced the number of benign tertian and quartan parasites, but as the crescents were unaffected the authors did not consider it worth while continuing the treatment. *W. F.*

*Though, as the above shows, this derivative of narcotine has no anti-malaria properties, it may be worth recalling that the 1895 Commission found that malaria was less prevalent among opium eaters; also, opium was in common use in the Fens up to comparatively recent times "to ward off ague." It is unlikely that a custom of such long duration should have no foundation in fact.—Ed.

GIEMSA (G.) & OESTERLIN (M.). Chemotherapeutische Studien auf dem Gebiete der Chinaalkaloide. [**Chemotherapeutic Researches on Cinchona Alkaloids.**]—*Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Vol. 37. No. 4. pp. 217–244 (5–32). With 1 fig. [42 refs.]

The results obtained from a chemical and therapeutic research carried on over a period of two years with two main objectives in view, to increase the antimalarial action of the alkaloids and to reduce the toxic effects.

Part I of the monograph deals with the chemotherapeutic investigations, and in Part 2 the results of the chemical researches are recorded.

In the chemotherapeutic investigations the authors worked with bird malaria (*Plasmodium praecox*) using the standard technique of ROEHL, except that 0·5 cc. instead of 1 cc. was administered as they found the birds frequently regurgitated the larger amount. In recording the efficiency of the substances tested the terms " range of action " or " strength of action " were employed. " Range of action " means the ratio of the smallest therapeutically active dose to the maximum tolerated dose, in quinine it is 1 : 4. The " strength of action " of the substance is determined by giving the substance to the bird during the incubation period, and, if effective, the parasites do not appear in the blood on the 6th to the 7th day after injection as in concontrols, but later, and the duration of this delay increases with the antimalarial activity of the drug. The results of the investigations are set forth in a table which shows that 70 substances were studied in detail. They found one substance particularly active as an antimalarial agent, C.77 (6-Methoxychinolin-8-azo-hydrocuprein). It had a " range of action " of 1 : 8.

The chemical portion of this valuable monograph is of highly technical character and should be consulted in original by those interested.

E. D. W. Greig.

TAREJEW (E.), EPSTEIN (H.), GANTAEVA (A.), RASKIN & BOLOTINA (A.). Essais thérapeutiques du plasmocide, dérivé synthétique de la quinoléine, dans le paludisme. [**Plasmocide, a Synthetic Derivative of Quinoline in Malaria.**]—*Bull. Soc. Path. Exot.* 1933. Oct. 11. Vol. 26. No. 8. pp. 1037–1046. With 1 fig.

This drug resembles plasmoquine in many respects.

Dr. O. MAGUIDSON and his colleagues at the Institute of Experimental Chemistry and Pharmacology have synthesized a number of anti-malarial drugs, which have been tested on birds by Professor I. KRITCHEVSKY. Therapeutic tests of seven of them have been made by the authors, and they have named the one which gave the most satisfactory results " Plasmocide " or " Antimalarine B." It is methyl-bis-salicylate of 6-methoxy-8-(-N-diethyl-amino-propyl-amino) quinoline ; a yellowish-brown powder insoluble in water. It is given in tablets containing 0·03 gram, which represents 0·01 gram of the pure base. The daily dose is 5 tablets a day, one every 4 hours. A course consists of 3 days' medication, followed by 4 days rest, continued for 4 to 6 weeks. In quartan, the drug acted very well and no relapses occurred during the course of treatment. In benign tertian, it proved less potent ; 20 per cent. relapsed while treatment was being continued, and in most of these cases it was necessary to give quinine. In malignant tertian, the

action was like that of plasmoquine, it destroyed the gametocytes but had very little action on the schizonts ; 83 per cent. relapsed during treatment, and 33·3 per cent. after it ; for the treatment of this infection it is essential to give quinine with the plasmocide. The authors state in their " conclusions " that the patients showed no signs of intolerance, but, in the report itself, 6·38 per cent. are said to have shown slight toxic symptoms, chiefly epigastric pain, and in one case it was necessary to give morphine. *W. F.*

Bovet (D.) & Demanche (L.). Nouveaux produits actifs dans le paludisme aviaire : une quinoléine de synthèse agissant sur les schizontes et sur les gamètes (F. 852). [**New Synthetic Active Products in Bird-Malaria, No. 852.**]—*Ann. Inst. Pasteur.* 1933. Oct. Vol. 51. No. 4. pp. 528–534.

The synthetic drug No. 852, also a derivative of quinoline, acts on both schizonts and gametocytes. Drugs like quinine and atebrin which are active in bird-malaria due to *P. relictum* are also active against the schizonts of human malaria; drugs like plasmoquine which are active in the malaria of rice-birds due to *Haemoproteus paddae* are active against the gametocytes of human malaria. In the course of their researches into the higher homologues of plasmoquine, the authors have found that if the diamine chain attached to the methoxyquinoline nucleus is lengthened, the gametocidal action is weakened while the schizontocidal action is strengthened. Proceeding on these lines, they have prepared 8-diethylamino-undecylamino-6-methoxyquinoline, or No. 852 F. This product not only acts as powerfully as atebrin on the malaria of canaries, but it also acts on the malaria of paddy-birds though not as powerfully as plasmoquine. The authors concluded therefore that it would have an action upon all forms of human malaria parasites, including gametocytes, and this has been borne out by chemical trials. It is less toxic than plasmoquine.
W. F.

Kikuth (W.) & Giovannola (A.). Zur Frage der medikamentösen Malariaprophylaxe auf Grund von experimentellen Untersuchungen an der Vogelmalaria. (**The Antimalarial Medical Prophylaxis according to Experimental Researches on Bird Malaria.**) —*Riv. di Malariologia.* 1933. July–Aug. Vol. 12. No. 4. pp. 657–674. [28 refs.] English summary (8 lines) p. 836.

In their experimental investigations the authors employed a special technique. They did not allow the mosquitoes (*Culex pipiens*), infected with two varieties of *Proteosoma* (*P. cathemerium* and *P. praecox*) to bite the canaries, as the results were very irregular in this method, but they dissected out the infected salivary glands and injected the sporozoites into the birds ; in this way they got 100 per cent. infection with *P. cathemerium*. The drugs were administered *per os* through a tube in accordance with the technique of Roehl. As a result of their researches the authors conclude that :—Neither quinine nor the two synthetic antimalaria drugs, plasmoquine and atebrin, can destroy in the tissues of the birds the sporozoites of *P. cathemerium* and *P. praecox*. None of these drugs can be regarded as causal prophylactics of malaria. Atebrin appears to have a " clinical " prophylactic action, which must be regarded as a therapeutic effect, because it develops during the slow excretion of this drug. *E. D. W. Greig.*

CHOPRA (R. N.), GUPTA (J. C.) & GANGULI (S. K.). **The Action of Some Synthetic Antimalarial Remedies on the Uterus.**—*Indian Med. Gaz.* 1933. Oct. Vol. 68. No. 10. pp. 558–561.

Malarcan and tebetren exert an oxytocic action, plasmoquine and atebrin do not.

The authors reached the following conclusions as the result of experiments on cats, rabbits and guineapigs :—The pregnant uterus is more susceptible than the non-pregnant to the action of anti-malarial drugs. Plasmoquine and atebrin in therapeutic doses are unlikely to exert an oxytocic action on the pregnant human uterus. Malarcan and tebetren may produce increased contractions in doses not very much larger than therapeutic doses. Large therapeutic doses of quinine are likely to increase the contractions of the pregnant uterus, and therefore, in pregnancy, small doses of about 5 grains every 5 hours should be prescribed. *W. F.*

FAIRLEY (N. Hamilton) & BROMFIELD (R. J.). **Laboratory Studies in Malaria and Blackwater Fever. Part I. Malaria.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. Nov. 30. Vol. 27. No. 3. pp. 289–314. With 5 graphs. [34 refs.]

There is no haemoglobinaemia or acidosis in malaria. The direct van den Bergh is negative ; the indirect shows hyperbilirubinaemia. Blood urea rises during fever, cholesterol declines. The anaemia is not megalocytic. The reticulocytes increase when the parasites are destroyed by drugs.

The authors conclude that there is no valid evidence of the occurrence of haemoglobinaemia in malaria. The appearance of stained films suggests that much of the haemoglobin is destroyed before the corpuscle ruptures during schizogony, and that damaged, parasitized cells are engulfed whole by the reticulo-endothelial system. A modification of Bloem's method was employed for the study of this question. The limit of sensitivity for the spectroscopic detection of haemoglobin in plasma was found to be 0·33 per cent., and the limit for methaemoglobin 0·665 per cent. For purposes of estimating haemoglobin in an unknown plasma, this was diluted until the alpha band in the spectrum just disappeared, and the degree of dilution was then multiplied by the standard figure of 0·33. In 28 cases of malaria with parasites in the blood, there was no haemoglobinaemia in 16, and only a trace in the remaining 12. In 53 controls there was none in 46, but there was a trace in 7, and the authors decided that the plasma haemoglobin must exceed 0·12 per cent. before it is significant of haemoglobinaemia in malaria.

The bilirubin content of the plasma was investigated in 30 M.T. and 20 B.T. cases by the van den Bergh test, with the result that neither immediate direct nor biphasic reactions were observed ; but as regards the indirect reaction this showed an increase above the normal limit of one unit of bilirubin in 19 of the 30 M.T. cases and in 13 of the 20 B.T. cases. This hyperbilirubinaemia may result from the disintegration of haemoglobin anywhere in the body—*e.g.*, phagocytosis in the reticulo-endothelial system—and does not necessarily indicate intravascular haemolysis, as some workers have thought. The hyperbilirubinaemia disappeared rapidly when specific antimalaria remedies were given.

SINTON and BAILEY reported that a condition of acidosis or lowering of the alkali reserve occurred in malaria. The authors examined 16

M.T. cases and 7 B.T. cases by van Slyke's method, with the result that they found no lowering of the CO_2 combining value of the plasma, except to a slight extent in two cases where it had been caused by vomiting. They therefore conclude that there is no acidosis in malaria, so far as decrease in the alkali reserve is concerned.

During the actual fever there is a rise in the blood-urea which is due to blood destruction and the accelerated katabolism associated with fever. In experimentally infected cases of malaria, the blood cholesterol declined when the parasites appeared, and increased steadily when they disappeared as the result of specific treatment. This is interesting because hypocholesteraemia is characteristic of pernicious anaemia; here, the cholesterol rises with specific liver treatment and the reticulocyte response which accompanies it.

On haematological grounds, there is good reason for doubting if uncomplicated malaria ever produces a true megalocytic anaemia like that of pernicious anaemia. In malaria, megalocytes are rare, the colour index is normal or reduced, and the average diameter of the corpuscle is not increased; if pernicious anaemia is suspected, the question can best be answered by a Price-Jones curve.

The authors studied the reticulocytes in unfixed blood stained with brilliant cresyl blue. The reticulocytes are identical with the polychromatic erythrocytes of Leishman-stained films. They are immature blood cells whose numbers indicate the activity of the bone marrow. Their normal number varies from 0·2 to 2 per cent.; in the cases of malaria with parasites in the blood which were investigated by the authors, they were from 0·6 to 10·9 per cent. Blood destruction in malaria is followed by compensatory hypertrophy of the red marrow which may replace the yellow marrow of the long bones; it is normoblastic in type, and thus differs from the megaloblastic degeneration of pernicious anaemia. From this red marrow the reticulocytes arise, and, following the destruction of malaria parasites by specific drugs, they swarm into the blood, and rise from the normal, up to 20 per cent. or more. The lower the blood count, the larger will be the area of erythroblastic tissue laid down, and the greater will be the reticulocyte response when once the parasites have ceased to exert their inhibitory influence on haematopoiesis. Increased blood production follows the destruction of the parasites, and proceeds quite independently of the administration of haematinics such as iron. *W. F.*

Machwiladze (Niko) & Kurpanova (M.). Ueber die diagnostische Bedeutung der Zunahme der Zahl der Retikulozyten bei Verordnung von Chinin ex juvantibus bei Malaria. [**Diagnostic Significance of Increase of Reticulocytes in Malaria after Quinine Administration.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. Nov. Vol. 37. No. 11. pp. 499–504. With 1 fig.

The enumeration of reticulocytes may be of assistance in the diagnosis of latent malaria.

The reticulocytes in cases of malaria were counted in the usual way in preparations stained with cresyl blue. The enumerations were done in the morning, twice, before the quinine administration, which was given intramuscularly twice daily in doses of 0·5 gm. for 7 to 8 days. The reticulocytes were enumerated daily. The authors conclude from their observations that:—In all forms of malaria with parasites in the blood an increase of the number of reticulocytes follows the administration of

quinine, the peak being reached about the 4th to the 5th day. In no other disease or anaemic condition did they observe an analogous action of quinine. Hence they conclude that the increase of the reticulocytes after quinine administration is specific for malaria. Consequently, the enumeration of reticulocytes may be of great help in the diagnosis of latent cases of malaria, particularly those without parasites in the blood ; for this purpose the enumeration of the reticulocytes should be made before the administration of quinine, and again 4 to 5 days after the administration. *E. D. W. Greig.*

Strickland (C.) & Roy (D. N.). **Malarial Infection of the Gut of *Anopheles stephensi* in Calcutta.**—*Riv. di Malariologia.* 1933. Jan.–Feb. Vol. 12. No. 1. pp. 57–69. With 6 figs. on 3 plates & 1 chart.

The authors believe that the " chitin bodies " of Brug are due to the deposition of chitin in zygotes and sporozoites which have died during their development within the mosquito. This chitinization is not an encystment to protect the living parasite from the host, but rather to protect the host from the dead parasite. [The numbers under some of the microphotographs have been accidentally transposed.] *W. F.*

Joukoff (N. M.) & Krassikova (V.). L'action du plasmocide sur l'infectibilité de l'*Anopheles maculipennis* pour le *Plasmodium vivax* et *P. falciparum.* [**Action of Plasmocide on Infectibility of *A. maculipennis.*]**—*Med. Parasit. & Parasitic Dis.* Moscow. 1933. Vol. 2. No. 1–2. pp. 65–72. [In Russian. French summary p. 72.]

The authors describe experiments on the prophylactic value of a new synthetic antimalarial preparation, " plasmocide " or " anti-malarin," produced in Russia [see Tarejew, above, p. 174].

The blood of cases of benign and malignant tertian malaria was first examined for parasites, batches of " wild " mosquitoes (*Anopheles maculipennis*) were then fed on the patients, and " plasmocide " was administered (6 doses of 0·015 gram : five on one day and one next day, 10 hours after the last dose). Two hours after each dose of the drug blood films were taken and a fresh batch of mosquitoes allowed to feed on each patient. In the experiment with B.T. 6 patients were used. The infection rate of the mosquitoes which was 72·7 per cent. (8 out of 11) before treatment fell to 18·3 (11 out of 60) after the first dose, and to 0 (39 mosquitoes) after the sixth dose. In the case of M.T., in which 7 patients were used, the infection rate in the mosquitoes before treatment was 13·3 per cent. (6 out of 45) ; after the first dose it fell to 9·3 (5 out of 54), and after the sixth to zero (74 mosquitoes). This reduction of the infection rate in the insect vector was not due to a corresponding decrease in the number of gametocytes in the blood of the patients, which was not affected by the treatment. The main effect of the drug is the inhibition of the development of the parasite in the mosquito. In the infected mosquitoes the number of öocysts and sporozoites is also reduced, as compared to the control series.

C. A. Hoare.

Barraud (P. J.). **A Method of making Slide Smears from Female *Anopheles*, for Examination for Sporozoites of Malaria Parasites, and of preserving the Mosquitoes for Reference.**—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 451–454. With 2 figs.

The author states that the method described combines the advantages of dissection of the salivary glands with those of Sergent's method for detecting sporozoites in the body-fluid. The paper is too detailed for summary. *W. F.*

Krishnan (K. V.), Smith (R. O. A.) & Lal (Chiranji). **Contributions to Protozoal Immunity. Part I. The Effect of Splenectomy on the Course of Malarial Infection in Monkeys.**—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 343–352. [13 refs.]

Immunity in malaria is a function of the reticulo-endothelial system, and removal of the spleen renders monkeys of highly tolerant species subject to severe and fatal infection.

The reactions of 14 splenectomized *M. rhesus* monkeys to malaria were compared with those of 27 non-splenectomized monkeys of the same species. Two out of seven non-splenectomized animals recovered without treatment, but all the non-treated splenectomized monkeys died. Treatment with quinine saved 80 per cent. of the normal monkeys but only about 10 per cent. of the splenectomized.

Malarial infections (*P. inui*) in normal *M. irus* and *M. radiatus* monkeys are almost symptomless and never fatal, but the inoculation with *Plasmodium inui* of 16 splenectomized monkeys of these species produced an acute fatal illness. Seven out of 10 untreated monkeys died, and also 2 out of 6 which were treated with quinine. The authors consider that immunity in malaria depends upon the functional efficiency of the reticulo-endothelial system. "Removal of the spleen, by interfering with these processes, converts latency into relapse, resistance into susceptibility and recovery into death."

W. F.

Chopra (R. N.) & Chaudhury (S. G.). **On the Electric Charge of Erythrocytes. Part II. Malaria.**—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 273–276.

The authors have found that the negative charge of erythrocytes collected from malaria patients and suspended in salt solution, is very variable; in some cases the charge is lower than the normal, in others it is higher. (See this *Bulletin*, Vol. 30, Brown, p. 830.) *W. F.*

Koch (Franz) & Vohwinkel (Karl H.). Ueber die Flockungsreaktion nach Henry bei Impfmalaria (Beitrag ueber die Rezidivgefahr). [**Henry's Flocculation Reaction in Inoculation Malaria. Danger of Transmission from Relapses.**]—*Deut. Med. Woch.* 1933. Dec. 1. Vol. 59. No. 48. pp. 1792–1793.

This investigation on the flocculation reaction was undertaken with reference to the warning recently expressed of the danger of the transmission of inoculation malaria by anopheles and of the relapse.

The authors do not discuss the technique of the reaction in detail, but refer to the paper of Kappus [this *Bulletin*, Vol. 30, p. 88]. They

employed as antigen iron albuminate No. 113, Merck. They studied 21 cases of inoculation malaria. All showed a positive reaction from the 7th rigor onwards. Usually the fever was stopped by quinine after the 8th rigor and in 8 to 10 days thereafter the reaction was negative in 100 per cent. of the cases. From their investigations and study of the literature they are of opinion that the undesired transmission of inoculation malaria is not a danger to the community. Cases recorded will not stand close scrutiny and are very unconvincing. They consider that inoculation malaria stands in a special relation to natural infection with benign tertian, because of the former's suceptibility to quinine, the rarity of relapse, and because small doses of quinine rendered a positive flocculation reaction negative in 100 per cent. of cases. *E. D. W. Greig.*

Chorine (V.) & Gillier (R.). Sur le mécanisme de la réaction de Henry dans l'infection paludéenne. [**The Mechanism of Henry's Reaction.**]—*C. R. Acad. Sci.* 1933. Oct. 23. Vol. 197. No. 17. pp. 950–952.

This reaction is governed by: (1) an increase of substances which are soluble in serum, but insoluble in distilled water; (2) the molecular concentration of the blood. It is due to a disturbance in the proportion of these two factors. The authors have already shown that melanin does not possess antigenic properties, and that surflocculence, or flocculation in the tubes without melanin, increases parallel with diagnostic reaction during the course of malaria.

In order to test the hypothesis that the reaction depends upon an increase of globulin, they added globulin to a negative serum and found that it then became positive; when heated for half an hour at 55°C. it became negative again. The reaction appears to depend upon the greater solubility of globulin in serum than in water. Other substances with the same property act in the same way; for example, the addition of lecithin will make a negative serum positive. Such substances are more soluble in salt solution than in water, and the addition of an electrolyte to a slightly positive serum will make it negative; removal of salts by dialysis, on the contrary, will tend to make a negative serum positive. During a malaria paroxysm, the potassium in the blood rises sharply with the destruction of many blood cells, and a positive reaction tends to become negative. The excess of potassium is quickly eliminated at the end of the attack, and the reaction is restored. The melanin appears to react simply as an indicator of the reaction. *W. F.*

Badensky (A.) & Bivol (E.). La réaction d'Henry dans le diagnostic du paludisme. [**Henry's Reaction in Diagnosis of Malaria.**]—*C. R. Soc. Biol.* 1933. Vol. 114. No. 29. pp. 224–225.

The authors studied the reaction in 95 cases of inoculation malaria. It was negative before the fever began, it was feebly positive during the early paroxysms, it became strongly positive after 7 or 8 had occurred, and it disappeared gradually under the influence of quinine.

W. F.

Kritschewski (I. L.) & Demidowa (L. W.). Das Phänomen der Melanoflockulation bei der experimentellen Vogelmalaria. [**Melanoflocculation in Bird Malaria.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1933. Vol. 80. No. 1/2. pp. 135–145.

The authors undertook the investigation to determine whether the reaction of Henry was a true immunity reaction with the formation of antibodies to the pigment, which is more or less related to that of the plasmodium, or whether this reaction was only an alteration of the physico-chemical properties of the human organism under the influence of the parasite, which has not been observed in the true immunological reactions known to us. For their researches they employed three species of birds, namely, *Spinus spinus*, *Acanthis linaria*, and *Serinus canarius*. Two different species of malaria parasite were used, *Plasmodium praecox*, and *Plasmodium cathemerium*. As a result of their studies the authors conclude that the phenomenon of melanoflocculation is a reaction between antigen, the melanine of the retina, and antibodies ; the latter are formed in the animal body by the action of the melanine of the malaria parasite.

E. D. W. Greig.

Stott (H.). **The Mechanism of Immunity in Malaria. Proof of the Phagocytosis of Malarial Parasites by Large Mononuclear Cells in Malaria.**—*Indian Med. Gaz.* 1933. Sept. Vol. 68. No. 9. pp. 507–510. With 8 figs.

The author reports two cases in which mononuclear phagocytes containing engulfed parasites were present in the peripheral blood. Both were cases of heavy subtertian infection with numerous sporulating forms in the peripheral circulation. He suggests that phagocytosis normally takes place in the fixed reticulo-endothelial cells which become free in the blood only in the severest infections. [See de Langen, this *Bulletin*, Vol. 29, p. 717, and J. G. Thomson, Vol. 30, p. 827.]

W. F.

Krishnan (K. V.), Lal (Chiranji) & Napier (L. Everard). **Cytological Studies of the Blood and Tissues in Kala-Azar and Associated Conditions. Part IV. The Large Mononuclear Cells in Monkey Malaria.**—*Indian Med. Gaz.* 1933. Feb. Vol. 68. No. 2. pp. 66–74. With 5 charts & 1 coloured plate.

It is here recorded that observations on monkeys suffering from malaria have shown that each of the three types of mononuclear cell occurring in the blood plays a part in the immunity process. The histiocyte is primarily responsible for the removal of damaged red cells from the peripheral blood. In malarial attacks it is the first cell to be stimulated and becomes more and more numerous during the destruction of red cells. When the infection subsides and becomes latent its numbers fall. In those cases in which the infection gains the upper hand the histiocyte percentage also falls. Following the histiocyte the cell of intermediate type with similar function is stimulated while finally the monocyte count increases. So long as the monocyte count remains high the malarial infection does not get out of hand. It seem probable that this cell has an indirect action associated with some humoral change in the serum which limits multiplication of the parasite in the body.

In a coloured plate are illustrated the various cells of the blood as revealed by the method of supravital staining employed in the investigation. *C. M. W.*

PANAGIA (Antoaino). Colesterinemia e reazione di Wassermann nella malaria. (**Cholesterinemia and Wassermann Reaction in Malaria.**) —*Riv. di Malariologia.* 1933. Sept.–Oct. Vol. 12. No. 5. pp. 873–881. [37 refs.] English summary (10 lines) p. 1064.

Three interconnected investigations are comprised in this article: (1) the amount of cholesterol in the blood of malaria patients; (2) the W.R. in malaria; and (3) the relation between the amount of cholesterol in the blood and the W.R.

Under normal conditions the amount of cholesterol in blood is taken as between 1·5 and 1·8 gm. per mille. Among 59 patients, the amount was found to be normal in 18, above normal (up to 3·0 per mille) in 20, and below normal (down to 1·1) in 21. There is nothing characteristic, therefore, in this respect. [See FAIRLEY and BROMFIELD, above, p. 176.]

As regards the W.R. in these patients, "all clinically free from syphilis," four gave a weak positive, five a marked positive, four others a doubtful reaction; *i.e.*, 4·7 per cent. only were positive.

Lastly, no correlation was made out between the amount of cholesterol in the blood and the W.R. From the detailed protocol it is seen that four patients with cholesterol within the normal limits gave a marked positive, while of five with an increase in cholesterol one gave a weak positive and four a doubtful reaction. *H. H. S.*

BOYD (George H.). **Host Fatigue and Feeding in their Relation to the Reproductive Activity of** *Plasmodium cathemerium* **Hartman.** —*Amer. Jl. Hyg.* 1933. Sept. Vol. 18. No. 2. pp. 295–322. With 14 figs.

The author's conclusions to these researches on canaries infected with *P. cathemerium*, are as follows:—

"1. Although reversal in the daily cycle of exposure of the host to light and darkness forms a very effective means of reversing the reproductive activity of *P. cathemerium*, these experiments indicate that the light itself is not of primary importance.

"2. The results of these studies do not seem to indicate that host fatigue plays any part in determining the definite periodicity which normally characterizes the reproduction of *P. cathemerium*.

"3. The taking of water by the host appears to have no effect upon the reproduction of these parasites.

"4. The factors associated with host feeding seem to exert considerable influence upon the reproductive activity of this parasite. These factors are difficult to control, and there are probably other factors involved, but these experiments seem to us to indicate that the feeding habits of the host bear an important relation to the definiteness of the periodicity of reproduction which characterizes these parasites." *W. F.*

MAJID (Syed Abdul) & SINTON (J. A.). **The Longevity of Females of** *Culex fatigans* **under Experimental Conditions, and the Duration of Malarial Infections in these Insects.**—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 455–466. [12 refs.]

Half the mosquitoes survived 100 days. One survived 210 days.

Ninety-nine *C. fatigans* were given a blood meal from a sparrow infected with proteosoma; they were then kept in a room with an

average temperature of 62·5°F., and a relative humidity between 60 and 80 within the mosquito-containers. Forty of the mosquitoes survived for 105 days. These forty were then kept at an average temperature of 70·5°F., with a rather lower humidity than before. Five mosquitoes survived until the 189th day, one up to the 196th day and one to the 210th. Active, but apparently non-infective, sporozoites were found as late as 166 days after the infecting feed, and non-motile sporozoites as late as 210 days. At lower temperatures, such as are employed by James, maturation of the parasites is slower and they remain infective for a longer period. *W. F.*

Rodenwaldt (Ernst). Kaart en determineertabel van de larven der anophelinen van Ned. Oost-Indië. [**Card and Identification Key of Anopheline Larvae of the Netherlands East Indies.**]—1 folding table & 2 folding plates. 3rd Edition. 1933. Weltevreden : Uitgegeven door den Dienst der Volksgezondheid.

The first edition of this work issued in 1927 (this *Bulletin*, Vol. 25, p. 815) described 16 species ; the second, 2½ years later, amplified this but the number described was only seventeen. The present, third, issue is considerably larger and more detailed. The author states in his preface that there have been of late years many new discoveries, especially in the eastern part of the archipelago and that on this account a new edition of his work was needed and not merely because the former was exhausted.

He describes in detail with large and clear illustrations 21 species, including this time rarer forms, because medical men now devote considerable time and care to the study of these larvae and the inclusion of rarer forms will no longer give rise to confusion but will be a welcome aid. For the same reason he considers certain characteristics which, with few exceptions, do not as a rule play a large part in differentiation of species, namely the costal palmate hairs ; these, he finds, a valuable group characteristic and serviceable, therefore, when but a few or damaged specimens are available. This is a useful point, he states, in distinguishing the larva of *A. parangensis* from that of *A. ludlowi-subpictus* ; again, the larva of *A. merancensis* resembles in all other respects *A. philippinensis* and can only be distinguished by these combs. By this means, too, *A. amictus* has been removed from its former grouping. They differentiate *A. hyrcanus* from all other species of Myzorhynchus and *A. anandalei* and *A. subpictus* in sweet water from the forms found in salt water.

Other distinctive points on which special stress is laid are the "shoulder hairs" and the bosses (wortelknoppen) on which they are inserted.

Finally, as regards the larva described as *probably A. leucosphyrus* var. *hackeri*, this has been described as a separate species in accordance with the opinion of the Antimalaria Service.

The drawings are clear and of such a magnification that the characters are well demonstrated and easily followed, although all the text is Dutch. *H. H. S.*

Fourie (L.). **Practical Aspects of Malaria Control in the Sugar Belt of Natal.**—*South African Health Officials' Assoc. Rep. Proc. 8th Congress, Pietermaritzburg, 5th, 6th, 7th & 8th June, 1933.* pp. 2–10.

This paper describes the creation in June 1932, of an organization, on the lines recommended by Professor Swellengrebel [this *Bulletin*,

Vol. 28, p. 981], consisting of 14 local Malaria Committees whose areas of jurisdiction cover the whole of the sugar belt in which malaria has become a grave menace during recent years.

The area involved is nearly a thousand square miles in extent. Four courses, lasting 5 or 6 days each, have been held for training the personnel of the committees in the methods of malaria prevention and about 50 Europeans attended. The area of operations is limited to the breeding places of *A. costalis*, and is restricted to a half-mile radius round human habitations. Oil has entirely superseded Paris green as a larvicide in Natal, but the author thinks that the latter is useful in newly-planted cane fields where oil may injure the crops, and also in native water-holes during dry weather. He recommends that antilarval measures should not be discontinued entirely during the off-season. He emphasizes the importance of checking all work, by searching for adult mosquitoes in houses. The results of the measures adopted are very promising. *W. F.*

Henrard (C.) & van Hoof (L.). Etude de facteurs épidémiologiques au cours d'un essai limite de prophylaxie antipaludique par la quinine et la plasmochine. [**Epidemiological Factors in an Attempt at Prophylaxis with Quinine and Plasmoquine.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. Oct. 30. Vol. 13. No. 3. pp. 267–284. With 1 plan.

The attempt failed and the failure is attributed to the difficulty of isolating the treated group.

This experiment was made in a somewhat isolated coolie camp on a coffee estate near Léopoldville. Another camp, 800 metres distant, served as a control. A river between the two camps was the breeding-ground of *A. costalis* the carrier. The splenic index was 50, and the parasitic index 62; 13·7 per cent. of 204 *A. costalis* were found to be infected. From the 18th March 1932, each coolie was given 8 grains of quinine and 0·02 gram of plasmoquine daily, and this treatment was continued—except that the quinine was reduced to 4 grains after April 6th—until June 26. The doses were given by an orderly who neglected his duty, but, nevertheless, only 14 per cent. of the coolies had schizonts at the end of the treatment, and gametocytes were found in none. The infectivity rate of anopheles was only 3·2 per cent. as compared with 13·7 at the beginning of the experiment, but the authors ascribe this to the dry season, because the index had sunk to 2·6 in the control camp. Two months after the conclusion of the experiment, the rains came on and the infectivity index of the anopheles in the test camp was as high as it had been before the coolies were treated with plasmoquine. The authors ascribe the failure to the difficulty of isolating the coolies sufficiently to prevent the introduction of infection. *W. F.*

Barrowman (Barclay). **Chemotherapy in Anti-Malarial Sanitation.**—*Malayan Med. Jl.* 1933. Sept. Vol. 8. No. 3. pp. 163–175. With 4 charts.

The author is a firm believer in mosquito control as opposed to drug control. He also considers that the treatment of patients with 30 grains of quinine for 10 days is useless.

He analyses the cost and efficiency of various methods of prophylaxis by drugs as tested on a large area of rubber and coconut estates situated on the west coast of the Malay Peninsula, and he compares the results with those of mosquito control over a half mile radius around habitations. His main conclusion is " that in Malaya, where malaria is potentially hyperendemic throughout the 12 months of the year, no method of chemoprophylaxis at present available . . . can offer itself to any degree, as an alternative to antimosquito measures, for the antimalarial sanitation of a population exceeding 80 persons. Results obtained by chemoprophylaxis in India and Ceylon where there is a definite season in each year when malaria is naturally absent cannot be applied to conditions in Malaya." For very small isolated populations, antimosquito measures are too expensive and drugs may be employed. He is no believer in the ordinary " short quinine " treatment of 30 grains a day for 10 days : it " is useless either as a means of the cure of the individual or as a sanitary measure." He has found a week's treatment with atebrin much more effective and cheaper than three weeks' treatment with quinine and plasmoquine or three months' treatment with quinine alone. " By the universal use of the short treatment with atebrin the malaria incidence on a mosquito-controlled estate would be reduced . . . the malarial incidence in all systems other than those including anti-mosquito measures is so high as to be a strong adverse factor to the commercial working of the estate, quite apart from the fact that the cost of the necessary treatment of the disease is higher than that of the adequate anti-mosquito measures." [See WALLACE, below, and RUSSELL, above, p. 160.] *W. F.*

WALLACE (R. B.). **Further Field Experiments with Plasmochin in Oiled and Unoiled Areas.**—*Malayan Med. Jl.* 1933. Sept. Vol. 8. No. 3. pp. 145–162. With 6 charts.

The author describes his further attempts to control malaria on a rubber estate by means of plasmoquine and quinine.

The coolies on four divisions were given quinoplasmine, 3 tablets daily for 14 days, just about the time of the greatest prevalence of *A. maculatus*, at the beginning of the malaria season. At the end of the 14 days small doses of plasmoquine were given, and were continued for 5 months, until the end of the malaria season. The doses on the several divisions were respectively : 0·01 gram plasmoquine every third day ; 0·02 gram plasmoquine and 4 grains of quinine twice weekly ; 0·02 gram plasmoquine daily ; 0·02 gram plasmoquine daily. The last division differed from the other three because, on it, all anti-larval measures were suspended. The drugs were administered by the dressers in charge of the divisions. There was a considerable movement of coolies about the estate, and they were frequently transferred from one division to another. On all the treated divisions the malaria rate remained lower than on the control. The daily dose of 0·02 gram on the division where oiling was suspended " appeared to be successful in preventing malaria during the time the drug was given, in spite of the fact that the breeding places of *A. maculatus* . . . were abundant." The cost of treatment in this division was $1.00 (2s. 4d.) a head per month. The effects of the treatment had vanished two months after it was finished. (See this *Bulletin*, Vol. 28, p. 135.) *W. F.*

DE MELLO (I. Froilano). **A Scheme for Malarial Sanitation in Rural Areas.**—Reprinted from *Antiseptic.* 1933. Sept. 4 pp.

In praise of mass treatment with plasmoquine and quinine.

Codal, an isolated village with 47 inhabitants, had a splenic index of 82·7. A treatment consisting of 0·03 gram of plasmoquine with 0·5 gram of quinine was given to each adult every day for eight days, and smaller doses were given to the children. Three shorter secondary courses with the same doses were given at intervals, and subsequently one day's treatment every week for 2½ months. Any stranger coming into the village from the neighbouring malarious areas received a course of treatment. The killing of adult mosquitoes and the application of Paris green to breeding places was also carried out. The splenic index fell from 82 to 27, and the daily sick rate from 32 to 2. The mass treatment with plasmoquine of all villages having a splenic index of over 50 per cent. has now been made compulsory in Portuguese India. *W. F.*

BRITISH MEDICAL JOURNAL. 1933. Nov. 18. pp. 919–920.—**Mass Treatment with Plasmoquine.**

Two tablets of plasmoquine, given once a week for two weeks, halved the amount of malaria among employees in Trinidad during the two succeeding months.

Dr. Grant R. GRIBBEN treated the employees of the Trinidad Lake Asphalte Operating Co., Ltd., with tablets of plasmoquine containing 0·01 gram of plasmoquine and 0·125 of quinine. The dose given to adults was two tablets once a week for two weeks; the doses for children were in proportion to their ages. The tablets were handed over to the heads of families on pay-day for administration to themselves and their dependents. There are two malaria seasons in Trinidad; the first at the beginning of July, the second at the end of September. In the latter half of September 1932, 6,856 tablets were issued to 2,142 people, but only 1,289 received the complete two weeks' treatment. During the two months which followed, the attendances at the dispensary, on account of malaria, were only about half as many as those of the same months in 1931. In the latter half of June 1933, Dr. GRIBBEN repeated the mass treatment, and in July there were only 66 cases of malaria as compared with 96 cases in July 1932; at the same time, there was an increase of 28 per cent. in the amount of malaria in the surrounding districts.

The world-famous Pitch Lake occupies the centre of a crater-like depression about 110 acres in extent. The surface is fairly hard and can be easily walked over, but a continuous movement goes on, which results in the formation of many wrinkles and folds; these become filled with water, but they are kept clear of larvae by a small fish, *Rivulus hartii* (*Cyprinodontidae*), which can crawl overland from one pool to another. *W. F.*

PECORI (G.) & ESCALAR (G.). La lutte contre le paludisme dans la campagne Romaine en 1932. [**The Campaign against Malaria in the Roman Campagna in 1932.**]—*Bull. Office Internat. d'Hyg. Publique.* 1933. Oct. Vol. 25. No. 10. pp. 1743–1746.

The means employed are: searching out and treating infected persons, antilarval and antimosquito measures, and prophylactic

quinine in those places which are still malarious. The incidence of malaria during 1932 was 2·66 per cent. The primary cases amounted to only 1·2 per cent. The splenic index in 6,508 school children was 6·2 per cent. Benign tertian was three times as common as subtertian. Quartan was very rare. The population of the Campagna, apart from the suburbs of Rome, is now 82,087. *W. F.*

Goré (Ramkrishna N.). **The Feather-Duster Mosquito-Trap. (A Simple Device for catching Mosquitoes in Houses.)**—11 pp. With 3 charts. 1933. Bombay: 82 Ghodbunder Road, Khar. [4 annas.]

The author describes and figures a simple device for trapping mosquitoes in houses.

It depends on the observation that mosquitoes settle in numbers on feather dusters, such as are sold in the Indian bazaars, and may be trapped by slipping a muslin bag over a duster placed with the handle in an upright bottle. The dusters are disposed about the house in the evening and between 10.0 a.m. and 2.0 p.m. next day the insects are trapped in the muslin bag carefully lowered over duster and bottle (see figure). The bag and handle of the duster

(*a*) Feather-duster, (*b*) Bottle, (*c*) Muslin bag held at the closed end preparatory to lowering it over duster and bottle.

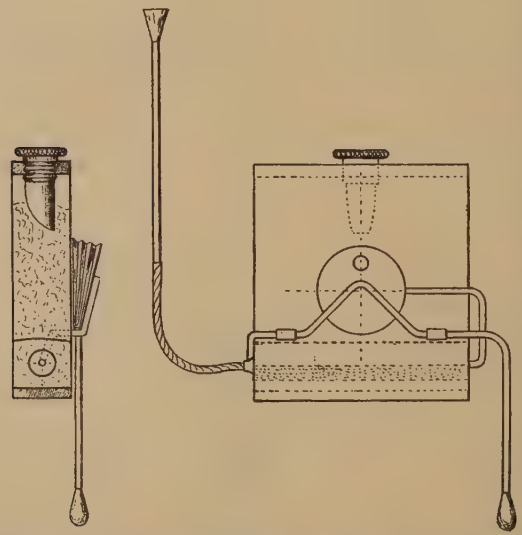
[Reproduced from "The Feather-Duster Mosquito-Trap" (Goré)].

are then grasped just above the bottle, from which they are lifted, the bag and duster are inverted and the duster is drawn out in such a way as to leave the insects behind. With some manual dexterity the same bag will collect from a series of dusters. The mosquitoes are then destroyed by heat or exposure to the sun.

The author has used these traps in his house in a suburb of Bombay for 15 months. Six traps daily have in 12 months accounted for 80,795 mosquitoes, the greatest number in one day being 1,015. The monthly counts are shown in a chart. In a later paper he will give details of genus and sex. [Many mosquito traps are described in COVELL'S "Malaria Control by Anti-Mosquito Measures." Nineteen references are given (see this *Bulletin*, Vol. 28, p. 1035).] *A. G. B.*

DE BENEDETTI (Augusto). Nota su di una modificazione per migliorare il funzionamento ed il rendimento delle macchine soffiatrici usate per lo spandimento del verde di Parigi. (**To improve the Function and Efficiency of Bellows used for the Dispersion of Paris Green.**) —*Riv. di Malariologia.* 1933. Sept.–Oct. Vol. 12. No. 5. pp. 897–900. With 1 fig. English summary (8 lines) p. 1064.

An improvement of the bellows used for the application of Paris green.



Bellows used for dispersion of Paris green, fitted with a punctured diaphragm to regulate the descent of the powder, thus avoiding any blocking of exit cylinder.

[Reproduced from *Rivista di Malariologia.*]

"The author has applied to the bellows a punctured diaphragm, which carries the larvicide mixture; thus is avoided the obstruction of the cylinder through which the powder is ejected by the draft caused by the pump. Besides, in the cylinder is a continuous descent of a limited amount of powder so that the dispersion is without interruption or loss. An economy of 50 per cent. is realized in the quantity of the larvicide mixture. The apparatus functions to the maximum with economy of time and labor. This modification is also useful for agricultural purposes." *A. G. B.*

Tilli (Pietro). Disanofelizzazione idrica mediante la calciocianamide. (**Larval Control through Calcium Cyanamide.**)—*Riv. di Malariologia.* 1933. July–Aug. Vol. 12. No. 4. pp. 722–730. English summary (5 lines) p. 838.

The author made trial of various chemicals as regards their larvicidal action; he found that the nitrates of ammonium or sodium and the sulphate of ammonium were effective only in a concentration as high as 8 per cent. He then tested calcium cyanamide (nitrolime), first as to its effects on the larvae of mosquitoes either obtained from the canals or bred in the laboratory; second as to its preventive effects, if any, on oviposition, and third, a field test. He found that in strengths of 0·14 to 0·03 per cent. (in different experiments) it had a larvicidal action, that when added to water it did not prevent deposition of ova, but many of them did not develop. In the field the effect depended considerably on the duration of application and was not to be compared with that of mineral oils or Paris green. *H. H. S.*

Bodenheimer (F. S.). Die Malaria als ökologisches Problem. Studien zur tierischen Bevölkerungslehre I.—*Folia Medicinae Internae Orientalia.* Jerusalem. 1933. May. Vol. 1. No. 2. pp. 135–168. With 10 figs. [2 pages of refs.] English summary.

Boyé. L'utilisation de l'avion à Madagascar dans la prophylaxie anti-paludique pour l'épandage du "Vert de Paris."—*Bull. Office Internat. d'Hyg. Publique.* 1933. Oct. Vol. 25. No. 10. pp. 1766–1768.

Brown (J. Youngson). African Children in European Reservations as a Reservoir for the Production of Sporozoite Infected Anopheles.—*West African Med. Jl.* 1933. July. Vol. 7. No. 1. pp. 81–82.

Chiang (W. L.) & Yang (C. S.). Prevalence of Malaria in the Mausolean District in Nanking. A Preliminary Survey.—*Chinese Med. Jl.* 1933. July. Vol. 47. No. 7. pp. 689–693.

Froes (Heitor). Endemiologia e profilaxia da malaria.—Reprinted from *Jl. dos Clinicos.* 1933. Aug. 15 & 30. Nos. 15 & 16. 39 pp. With 11 figs.

Hasselmann (C. M.). Therapeutical Notes on Atebrin, Plasmoquine (Plasmochin) and Yatren: a Critical Evaluation.—Reprinted from *Rev. Filipina de Med. y Farmacia.* 1933. Aug. Vol. 24. No. 8. pp. 359–367. [42 refs.]

Krishnan (K. V.). Observations on the Mode of Action of Quinine in Malaria.—*Indian Jl. Med. Res.* 1933. Oct. Vol. 21. No. 2. pp. 331–342. [10 refs.]

de Langen (C. D.). Enkele beschouwingen over de medicamenteuze behandeling en prophylaxe der malaria.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1933. Sept. 12. Vol. 73. No. 19. pp. 1154–1161.

Lasnet. Organisation et fonctionnement du service antipaludique en Algérie.—*Bull. Office Internat. d'Hyg. Publique.* 1933. Oct. Vol. 25. No. 10. pp. 1747–1765.

Lega (G.) & Casini (G.). L'azione della chinina e della plasmochina sui gametociti della malaria. (The Action of Quinine and Plasmoquine on Malarial Gametocytes.)—*Riv. di Malariologia.* 1933. July–Aug. Vol. 12. No. 4. pp. 701–707. With 2 figs. English summary p. 837.

Lucherini (Tommaso). Aumento di volume della milza nel periodo preaccessuale dell' infezione malarica primitiva inoculata a scopo terapeutico. (Spleen Increase during the Period preceding the Paroxysm of the Therapeutic Malaria.)—*Riv. di Malariologia.* 1933. July–Aug. Vol. 12. No. 4. pp. 718–721. English summary (4 lines) p. 838.

Manca (Serafino). L'azotemia nella malaria. (Azotemia in Malaria.)—*Riv. di Malariologia.* 1933. Sept.–Oct. Vol. 12. No. 5. pp. 848–858. [11 refs.] English summary (7 lines) p. 1063.

Manson-Bahr (Philip). Malaria and its Effects.—Reprinted from *Practitioner*. 1933. Aug. Vol. 131. pp. 124–135. With 3 charts.

Moretti (P.). Contributo allo studio della terapia della malaria con l'atebrin.—*Riv. Sanitaria Siciliana*. 1933. Oct. 1. Vol. 21. No. 19. pp. 1462, 1465–68, 1471–73. English summary (2 lines).

Morin (Henry G. S.), Moreau (P.) & Toumanoff (C.). Recherches sur le paludisme au Tonkin. II.—Bassin du Si-Kiang.—Region de Lang-Son–Cao-Bang.—*Bull. Soc. Méd.-Chirurg. Indochine*. 1933. May. Vol. 11. No. 3. pp. 256–290. With 1 chart. [14 refs.]

Morishita (Kaoru), Miyahara (Hatsuo) & Ishioka (Hiozo). Studies in the Treatment of Malaria. X. The Effect of Alkali-Therapy (a Modification of Sinton's Method) in Benign Tertian Malaria.—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1933. Sept. Vol. 32. No. 9 (342). [In Japanese pp. 1226–1236. [49 refs.] English summary pp. 120–121.]

Morishita (Kaoru), Miyahara (Hatsuo) & Ishioka (Hiozo). Studies in the Treatment of Malaria. XI. Experimental Treatment with Plasmoquine (IVth Report) : Simplification of the Use of Plasmoquine (Experiments with our P.Q.A. Method).—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1933. Sept. Vol. 32. No. 9 (342). [In Japanese pp. 1237–1247. [13 refs.] English summary pp. 122–123.]

Morishita (Kaoru), Miyahara (Hatsuo) & Ishioka (Hiozo). Studies in the Treatment of Malaria. XII. On Atebrin, a New Remedy for Malaria, with Notes on Our Preliminary Experiments with it.—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1933. Sept. Vol. 32. No. 9 (342). [In Japanese pp. 1248–1254. [11 refs.] English summary pp. 123–125.]

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Russell (Paul F.). The Value of an Animal Barrier in Malaria Control.—Reprinted from *Science*. 1933. Aug. 4. Vol. 78. No. 2014. pp. 101–102.

Vialatte (Ch.). Hémorragies gastro-intestinales au cours d'un accès de paludisme.—*Arch. Inst. Pasteur d'Algérie*. 1931. June. Vol. 9. No. 2. pp. 349–351.

Zaporojan (E.). Monografia malariei în circumscripţia Drăgăneşti, jud. Balţi, de anul 1931.—*Rev. Igienă Socială*. Bucharest. 1933. Oct. Vol. 3. No. 10. pp. 595–601. French summary.

Zimmermann (Edmund). Spitzengangrän bei Malaria.—*Deut. Med. Woch.* 1933. Dec. 29. Vol. 59. No. 52. pp. 1916–1918. With 2 figs. [11 refs.]

HEAT STROKE.

MORTON (T. C. St. C.). **The Aetiology and Treatment of Heat Exhaustion and Heat Hyperpyrexia, with Special Reference to Experiences in Iraq.**—*Proc. Roy. Soc. Med.* 1932. June. Vol. 25. No. 8. pp. 1261–1271 (United Services Sect. pp. 19–29). With 4 figs.

A study of a series of cases of heat exhaustion and heat hyperpyrexia occurring during a severe heat wave, with a discussion on aetiology, clinical symptoms, treatment, and prophylaxis.

Twenty-seven cases of heat exhaustion and three of heat hyperpyrexia occurred in Hinaidi where there was a low degree of humidity throughout, but a shade temperature which reached 120° on three days. The main symptoms shown by the cases of heat exhaustion were : vomiting (18) ; dizziness (13) ; constipation (11) ; cramp (6) ; suppression of urine (4) ; anidrosis (3). The author considers that there is no hard-and-fast line between severe heat exhaustion and heat hyperpyrexia, for heat exhaustion of the severe acidosis type, if untreated, will pass on to the complete clinical picture of hyperpyrexia. The treatment found effective for heat exhaustion was : (i) Preliminary purgation and treatment for shock ; (ii) the administration of the following mixture hourly for 24 hours—glucose, 1 drachm ; sod. bicarb., 15 grains ; water to 1 oz. If not well tolerated, pot. cit., 25 grains was given instead. When neither of these was retained, about 1½ pints of 2 per cent. sod. bicarb. in saline, sometimes combined with 5 per cent. glucose, was given intravenously. The beneficial effect of the intravenous injection is described as dramatic.

These intravenous injections gave disappointing results in heat hyperpyrexia, where the indications are to reduce the temperature as effectually as possible. The essential factor was found to be the provision of a specially cooled ward, and a considerable measure of success was achieved. The radiator of a Leyland lorry was kept filled with ice, and the fan-driven air was passed by means of a tunnel into a one-bedded bunk. By this means a constant temperature of 82° was obtained when the general ward temperature rose to 95°.

To prevent the onset of heat hyperpyrexia in fever cases in hospital, the author recommends : (1) Provision of an artificially cooled ward ; (2) Potassium citrate lemonade made by adding 10 to 15 grains of pot. cit. to a glass of home-made lemonade. A pint of this to be taken thrice daily. This latter is recommended also as a general prophylactic during a heat wave. *W. P. MacArthur.*

TALBOTT (John H.) & MICHELSEN (Jost). **Heat Cramps. A Clinical and Chemical Study.**—*Jl. Clin. Investigation.* 1933. May. Vol. 12. No. 3. pp. 533–549. With 1 fig. [26 refs.]

This paper is a clinical description of five cases of heat cramp with a discussion of a chemical study of blood and urine. It is argued that the etiological factor is a loss of base, chlorides and water from the body, without adequate replacement.

The authors' chemical observations indicate that the body tissues of patients with heat cramp contain hypotonic fluid, not from excess of water but from depletion of total base and chlorides. In this series of cases, the reduction in serum chlorides varied from 2 per cent. to

10 per cent. below the accepted normal minimal value, and was proportionate to the severity of symptoms. This deficiency was further evidenced by the marked retention of salt by the body early in recovery, and in one patient an intake of 45 grams of sodium chloride in 42 hours was accompanied by a urinary excretion of only 4 grams.

Owing to the loss of salt and water from the body and the concomitant replacement of water only, there is a lowering of the chloride level beyond the normal range. The authors believe that when a critical level for the chlorides is reached in working individuals muscle cramp will occur, and that the critical chloride level is a function of individual susceptibility, acclimatization and the length of the prodromal period.

Intravenous injections of normal saline in 5 per cent. glucose with an exclusive milk diet during the acute stage, were found satisfactory in the treatment of the cases studied.

Heat cramp may be prevented by providing a daily supply of salt greater than that lost in the sweat. This amount may be determined from the appropriate quantity of chloride excreted in a 24-hour urine specimen. The authors consider that less than 3 grams of salt per day in the urine does not provide for a satisfactory margin of safety.

W. P. M.

Mills (C. A.) & Ogle (Cordelia). **Climatic Basis for Susceptibility to Heat Stroke or Exhaustion.**—*Amer. Jl. Hyg.* 1933. May. Vol. 17. No. 3. pp. 686–696. With 4 maps.

A study of the adaptation of experimental animals to environmental temperature conditions is here compared with a statistical analysis of heat stroke and heat exhaustion as occurring in the United States of America.

The authors consider that the experiments detailed in this paper demonstrate that adaptation to constant heat renders animals more resistant to excessive heat, but markedly reduces their ability to increase combustion and keep warm under chilling conditions. Constant cooling, on the other hand, while making animals much more sensitive to excessive heat, increases their ability to withstand chilling. Most surprising, though, is the response of animals that live for two-thirds of the time at a high temperature, but are chilled daily for a few hours. These animals show a very active heat production to meet chilling emergencies, but are least able to endure a high temperature, even though it be only a few degrees higher than that to which they have been exposed for the greater part of each day.

It is argued from these experimental results that the differences in susceptibility to excessive heat admittedly shown by the inhabitants of different parts of the United States depend on variations in metabolic activity, and that these variations correspond with the type of climatic stimulation to which the people of the several regions are subjected.

W. P. M.

Shattuck (George C.) & Hilferty (Margaret M.). **Causes of Deaths from Heat in Massachusetts.**—*New England Jl. of Med.* 1933. Aug. 17. Vol. 209. No. 7. pp. 319–329. With 1 fig.

A discussion of the factors which influence deaths associated with heat in Massachusetts.

The authors conclude that "sunstroke" and "heat stroke" are indistinguishable clinically and that both of these terms should be replaced by "heat hyperpyrexia." The type of response to exposure to heat shows a definite correlation with age. Hyperpyrexia is far more common than exhaustion between the ages of 20 and 59, but heat exhaustion predominates after 60 years of age. As contributory causes of death from heat, diseases of the circulatory system stand first by a large average. This fact suggests that the circulatory system suffers particularly from the effects of excessive heat, and that the correlation of heat deaths with increasing age is due to progressive diminution of adaptability of the circulatory system to stress of this kind. *W. P. M.*

VAN ZWALENBURG (C.). **Dehydration in Heat Exhaustion and in Fatigue.**—*California & Western Med.* 1933. May. Vol. 38. No. 5. pp. 354–358. [32 refs.]

The author's theme is "Drink more water," and to the effects of dehydration he attributes heat exhaustion and fatigue following muscular exertion.

For the average person under moderate strain of mental and physical exercise, six to eight glasses of water daily are recommended. Two or three times this quantity is required by workers under conditions of heat such as are encountered in steel mills, foundries, hot mines and stokeholds of vessels. While in deserts in the tropics, the daily intake of water should amount to about thirteen litres in order to preserve an adequate reserve in the tissues. [The author does not consider the depletion of sodium chloride caused by excessive sweating.]

W. P. M.

MARSH (Frank). **Further Studies in "Heatstroke."**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. Nov. 30. Vol. 27. No. 3. pp. 255–267. With 2 graphs (1 folding). [12 refs.]

This paper, which cannot be summarized satisfactorily, deals with blood and urine chemistry in normal people, and blood chemistry in experimental heat stroke.

The author's experiments support the belief that in non-sweating laboratory animals hyperthermia is accompanied by a rise in blood lactic acid and a fall in plasma bicarbonate, which changes are accompanied, in the case of sweating man, by a fall in blood chloride. It is not clear how hypochloraemia interferes with sweating; possibly the sweat glands are unable to secrete sweat when the blood chloride is low, or, a low blood chloride may induce a secondary reduction in blood volume. A patient with his blood salt low and his bodily salt reserves exhausted will thirstily drink any available water. The blood volume is rapidly restored to its former low level, or even lower, by polyuria and a quick burst of sweating with further loss of chlorides. The vicious cycle can be broken only by the ingestion of salt.

W. P. M.

UNION OF SOUTH AFRICA. ANNUAL REPORT OF THE DEPARTMENT OF PUBLIC HEALTH YEAR ENDED 30TH JUNE, 1933. [**Heat Stroke.** pp. 18–19.]

Natives recruited for the South African mines from tropical areas are only half as susceptible to heat stroke as those from further south.

New boys are now acclimatized before being put to work at deep levels.

"During the year 20 fatal cases of heat stroke were reported from deep mines in the central and eastern Witwatersrand areas. Nine mines were involved in these deaths. This makes a total of 130 deaths from this cause on the mines since 1924, in which year a single death was reported from a deep level mine.

"A review of these cases showed that the view previously expressed regarding tribal acclimatisation is confirmed. In Table F the cases are shown according to the region from which the boys were recruited. The first column of figures shows the actual number of deaths. In the second column the deaths are expressed in proportion to the numbers of boys from each region working in the deep levels where the wet bulb thermometer records a temperature of 86°F. or over; it is in these levels that the great bulk of the cases occur. It will be seen that the natives recruited from the cold heights of Basutoland are nearly twice as susceptible as the tropical natives recruited from Portuguese territory. The Eastern Cape Province natives take an intermediate place. It would appear, therefore, that natives recruited from latitudes nearer the equator have a decided advantage in deep level mining over those from further south. Their rare deaths are an extreme expression of this advantage. This advantage must also obtain in less easily assessed ways such as greater working efficiency and lessened susceptibility to disease.

TABLE F.—*Fatal Heat Stroke Cases on the Witwatersrand Mines, 1924 to June, 1933.*

Area of Recruitment	Number of Deaths	Rate per 10,000 of the average number from each region working in hot zone
Basutoland	35	121
Eastern Cape	52	108
Mozambique	33	65
Other Areas	10	—
Total ...	130	

"The importance of local acclimatisation and individual susceptibility is clearly brought out by the figures. Of the 130 cases, 87 collapsed during the first or second shift worked in the hot place. All the deep level mines have now adopted a system of acclimatisation of new boys before putting them on the hard work in hot zones. Various methods have been adopted. The most satisfactory is that of putting the boys on to light work in a moderately warm place, followed by hard work in that place, then light work in the hot place. Light work is best arrived at by issuing only one shovel to every two boys and instructing them to hand over the shovel to another boy on the slightest fatigue. This acclimatisation is usually spread over a period of a fortnight. Heat collapse only exceptionally occurs in boys who have served in an acclimatisation gang; in such cases evasion of proper acclimatisation is generally elicited on investigation.

"In addition to acclimatisation elimination of boys specially susceptible to heat is now carried out on two mines of the Central Mining Rand Mines Group. The method adopted for elimination of such susceptibles consists of setting all recruits to do muscular work in a specially constructed chamber the atmosphere of which is kept saturated with moisture at a temperature of about 94°F. The rise of body temperature under these conditions makes it possible to assess the efficiency of the physiological cooling mechanism. The recruits are divided into three groups according to their reaction in the chamber. Those who show no susceptibility to heat in the chamber served an acclimatisation period of only 5 days, those slightly susceptible 7 days, those markedly susceptible 14 days. This chamber test has already fully justified itself. At the City Deep Mine where it is in full working there has not only been a reduction in the number of heat stroke cases, but also a great saving in working shifts on the mine." [See also this *Bulletin*, Vol. 29, p. 798.] *A. G. B.*

SLEEPING SICKNESS.

DUKE (H. Lyndhurst). **Studies on the Factors that may influence the Transmission of the Polymorphic Trypanosomes by Tsetse. IV. On the Spontaneous Disappearance of Flagellates from an Infected Glossina. V. On the Effects of Temperature. VI. On the Duration of the Biological Cycle in Glossina.**—*Ann. Trop. Med. & Parasit.* 1933. Oct. 21. Vol. 27. No. 3. pp. 431–435; 437–450; 451–467.

iv. An observation is recorded, which, in the author's view, seems to confirm an opinion expressed by BRUCE *et al.*, 1915, viz.: "It must, therefore, be held as probable that an infective fly, with presumably both salivary glands and alimentary tract swarming with trypanosomes, can lose all these flagellates and become non-infective."

A batch of laboratory-bred *G. palpalis* was fed for two days on a monkey infected with *T. gambiense*, and then, after being nourished for 16 days on a clean fowl, on several healthy monkeys, all of which became infected in the course of time. On the 43rd day of the experiment the remaining flies were killed and dissected, and in four flagellates were found to be swarming in both the guts and salivary glands. Another male fly, which was dead when removed from the box before its companions had been killed, revealed on dissection a state of affairs which the author had never before seen in ordinary transmission experiments, but which was reminiscent of the effects of feeding infective flies on arsenic-containing blood. This fly had died a natural death and had not fed for some days previous to its death. The intestine was empty of blood, although both glands were found to be crammed with trypanosomes, all of which were motionless and apparently dead, although unaltered in form; no trace of trypanosomes was found in the alimentary canal. Duke's experience convinces him that the fact that the fly had been dead overnight could not be held responsible for this remarkable phenomenon. He believes that the observation suggests that a trypanosome infection may die out from the alimentary canal in Glossina, and that indeed in this particular fly the gut had been cleared of trypanosomes for at least 3 or 4 days previous to its death. He furthermore considered it probable that the flagellates in the glands of this fly had died before its death, and that they would finally have disappeared, either by absorption or ejection, had the insect survived for a sufficient period after their demise.

Although it is highly probable that the phenomenon is of very rare occurrence in the ordinary conditions of experiment or in nature, the possibility of its occurrence must be borne in mind by those engaged in trypanosomiasis research.

v. In this paper Duke has examined the effect of temperature on the development of trypanosomes in *Glossina palpalis*.

The author commences by reviewing the literature of the subject beginning with the observations of KINGHORN and YORKE (1912), who found that "whereas the earlier stages of the cycle may take place at comparatively low temperatures, such as 60°F., for the invasion of the salivary glands high temperatures such as 75°F. to 85°F. are necessary." After referring briefly to the records of BRUCE *et al.* (1915) and of LLOYD (1930), the author discusses in detail TAYLOR'S recent experiments (1932) from which it is claimed that increasing

the temperature to 37°C. very greatly increased the infection rate of *G. tachinoides* [this *Bulletin*, Vol. 30, p. 105].

An account is then given of Duke's own carefully controlled experiments on this subject. Every test consisted of a pair of boxes, each containing at the outset about 50 *G. palpalis*. The two boxes of each pair were fed, one immediately after the other, on the infecting animal. One box was then placed in the incubator and the other kept in the laboratory. The experiment was divided into two series. In the first the incubator was kept at 86–88°F., and in the second at 95–98°F. Other details are given, but cannot be referred to here; suffice it to say that the laboratory maintained, and the incubator maintained, flies were otherwise subjected to exactly the same conditions. The trypanosomes used were *T. brucei*, *T. gambiense*, and *T. rhodesiense*.

The results of these two series of experiments are set forth in a couple of tables and the data obtained were subjected to examination by the formula $X^2 = \int \frac{(x-m)^2}{m}$. For Series I (laboratory temperature and incubator at 86–88°F.), the value for $X^2 = 2{\cdot}2404$. In Series II (laboratory temperature and incubator at 95–98°F.) the corresponding value = 5·0391. From this Duke concludes that whereas the difference between the two values in Series I may well be due to chance, in Series II the higher temperature is in all probability responsible for the greater infection rate shown by the flies.

Taylor considered that the increased infection rate in the incubated flies is due to the beneficial effect of high temperature on the trypanosome, helping it in its early efforts at multiplication and establishment in the fly. Duke believes that his experiments (Series II) show this explanation to be inadequate, and that the influence of the higher temperature on the fly itself must be also taken into account. Previous work has shown that *G. morsitans* is about twice as good a transmitter of the trypanosomes of man as is *G. palpalis*, and the work of Lloyd and of Taylor suggests that *G. tachinoides* is in certain circumstances even more efficient. Duke considers that differences of the order obtained by him are more easily explicable on the hypothesis that the higher temperature acts through the tsetse fly by affecting its physiological processes in some way favourable to the trypanosome. Duke contrasts in detail the climatic conditions of Nigeria with those of Entebbe, and points out that the differences between life in the incubator at 95–98°F. and that in the laboratory, or in the natural environment of the fly, is very much greater in Uganda than in Nigeria. With *G. palpalis* exposure to 36–37°C. causes a slight increase in efficiency, an increase that may, perhaps, represent the direct effect of the higher temperature on the blood trypanosomes during their first few days in the alimentary canal of the fly. To *G. tachinoides* 37°C. is a temperature well within its normal experience in nature, and brings out to the full its latent capacity to transmit the trypanosome.

vi. As the result of an extensive review of the literature and of an analysis of the accumulated data of his own work during many years at Entebbe, Duke reaches the conclusion that it is very exceptional for the biological cycle of man's trypanosomes in Glossina to take more than 30 days for its completion; as a rule, 25 days or less are required.

The first part of the paper is devoted to a review of observations bearing on the length of the cycle of *T. gambiense*, and to a less extent,

of *T. rhodesiense*, in different parts of Africa, including an account of 30 different strains of *T. gambiense* which have been studied at Entebbe since 1926. The second part is devoted to a consideration of trypanosome infections (*T. gambiense* and *T. rhodesiense*) in tsetse flies (*G. palpalis* and *G. morsitans*), which have lived 30 days or longer after their first meal on an infected animal, these infections being restricted to the alimentary canal of the fly and not involving the salivary glands. Duke considers that this information has a definite bearing on the whole question of the transmissibility of trypanosomes by Glossina. He points out that an important point of divergence between TAYLOR and himself is that, whereas the former believes that once a fly is infected in the proventriculus, it is merely a matter of time before the glands also become infected, he, Duke, believes that in all but exceptionally transmissible strains there will always be a certain number of flies in which no matter how long they live the glands will never become infected.

In a very lengthy table Duke has accumulated a vast amount of data bearing on this subject. The table gives information regarding the trypanosome used, the infecting animal, the age (after the infecting feed) of the flies on dissection, the day on which the earliest gland infection was found by dissection, the days on which "gut only" infections were found on dissection, and finally the earliest evidence of infectivity of flies acquired by feeding them on clean animals. This table shows that a fly may have its alimentary canal infected with a trypanosome during 5 to 7 weeks of laboratory service without becoming infective.

The general conclusions reached from this stage are :—

"(1) It is very exceptional for the biological cycle of man's trypanosomes in Glossina to take more than 30 days for its completion. As a general rule, 25 days or less are required.

"(2) With the majority of East African strains of *T. gambiense* there will always be a certain number of individual infected flies in which trypanosomes never reach the salivary glands, no matter how long the flies live after their infecting feeding." *W. Yorke.*

LESTER (H. M. O.). **The Characteristics of Some Nigerian Strains of the Polymorphic Trypanosomes.**—*Ann. Trop. Med. & Parasit.* 1933. Oct. 21. Vol. 27. No. 3. pp. 361–395. [46 refs.]

This very interesting paper gives valuable information regarding the various characters exhibited by a considerable number of Nigerian strains of polymorphic trypanosomes, and ends with a discussion regarding the relationship of *T. brucei*, *T. gambiense* and *T. rhodesiense*.

Among the considerations which induced Lester to undertake this work are : (1) that in Eket, Southern Nigeria, sleeping sickness is very mild, whilst in Northern Nigeria it may be either mild, as in the southern portion where *G. palpalis* is the chief vector, or more virulent as in the north where *G. tachinoides* is the chief vector ; (2) that from time to time medical officers have reported cases resistant to arsenical treatment ; and (3) that great differences exist in the way in which different strains from man behave in small laboratory animals.

Origin of strains.

The first series of strains were obtained from untreated patients attending Gadau Dispensary. These were people who had come

from the big epidemic area to the north of Gadau. Whilst some localities in this area are infested with *morsitans*, this fly tends to be localized to a great extent, so that the ordinary farmer does not come into close contact with it. *G. tachinoides* is obviously the chief vector of trypanosomiasis in the area. About 10 per cent. of the population is infected with the disease, and in some villages infection rates of 60 to 70 per cent. have been recorded. During the last two or three years about 10,000 cases of sleeping sickness have been treated from the area.

The other group of strains was obtained from Ayu district, Jemaa division of Plateau Province. Here the infection rate is about 5 per cent., and the chief vector is *G. palpalis*. These Gadau and Ayu strains were compared with 4 *T. brucei* strains isolated in the Gadau district and with two old laboratory strains of *T. gambiense* and *T. rhodesiense*, which had been kept for many years in London.

History of strains.

The Gadau and Ayu strains were isolated by the intraperitoneal injection of 5 cc. of blood from untreated sleeping sickness patients into *Macacus rhesus*. From the monkeys the strains were passed into guineapigs, and during the course of these investigations were maintained in guineapigs by syringe passage. Strains Gadau 1 to 4 were isolated in May, 1930, Gadau 5 in July, 1929, Gadau 6 in October, 1930, and Gadau 7 in January, 1932. The Ayu strains were isolated in April, 1931, and were used by Taylor (1932) for a series of cyclical transmissions in guineapigs, after which they were handed over to the author. Ayu 5, 7, 8 and 11 had been transmitted through *G. tachinoides*, and Ayu 6 had undergone one transmission by *morsitans*. The old London *gambiense* strain had been isolated from a patient from Nigeria in November, 1921, and the *rhodesiense* strain from a Luangwa Valley patient in January, 1923. Strain *Brucei* I was isolated from wild *G. morsitans* in 1928, and had been maintained since in a series of dogs and monkeys. *Brucei* 2 was isolated from wild *G. morsitans* in May, 1930, and has been since maintained in dogs and guineapigs. *Brucei* 3 was obtained from a naturally infected dog in November, 1932, and *Brucei* 4 from wild *G. morsitans* at the same time; both these strains have been maintained in guineapigs.

Each of these strains was then examined as regards its virulence in small laboratory animals, the occurrence of posterior nuclear forms, its susceptibility to tryparsamide, and its reaction to human serum. Full details of this work are given, and the results are summarized in the table, below, p. 200.

A number of human inoculation experiments were performed with Strain *Brucei* 4. Three Europeans and 40 natives were injected with blood from a rat infected with this parasite. The amount of blood given to each volunteer contained approximately 10 million trypanosomes. Immediately prior to inoculation the strain was tested *in vitro* against normal human serum, which was found to destroy the trypanosomes within 3 to 4 hours. As was anticipated the results were negative in every case.

Lester records that in 1932, when making a strain of *brucei* resistant to human serum in mice, he noticed that a strain completely resistant in mice to a dose of 1 cc. of normal human serum showed no signs of this resistance when tested *in vitro*. This finding was not reported at the time, but it has since been confirmed with another *brucei* strain. Strain *Brucei* 4 was maintained in mice which were treated with increasing intraperitoneal injections of normal human serum, until such time as it had become resistant in the mouse to a dose of 2 cc.

A summary of the characteristics of the various strains.

Strain	Virulence in small laboratory animals	Occurrence of posterior nuclear forms	Dose of tryparsamide required to clear trypanosomes from the peripheral blood, gm. per kilogram	Reaction to human serum
Gadau 1	Low virulence	Normal	Greater than ·04 gm.	Insensitive
,, 2	Normal	,,	Less than ·04 gm.	,,
,, 3	,,	Numerous up to 15 per cent.	,, ·04 ,,	,,
,, 4	,,	Normal	·004	,,
,, 5	,,	Up to 4·5 per cent.	Less than ·04 gm.	,,
,, 6	Virulent	Numerous up to 23 per cent.	·08	Sensitive 3 hours
,, 7	Normal	Normal	·05	Insensitive
Ayu 5	,,	Numerous up to 17 per cent. in white mice	·008	,,
,, 6	Virulent	Numerous up to 29·4 per cent.	Greater than ·25 gm.	Sensitive 3 hours
,, 7	Normal	Normal	·06	Insensitive
,, 8	,,	,,	·14	,,
,, 9	,,	,,	·06	,,
,, 11	,,	,,	·05	,,
London *gamb. T.*	Virulent	—	Less than ·04 gm.	Sensitive 3 hours
London *rhod. T.*	,,	—	Greater than ·25 gm.	,, ,,
Brucei 1	,,	—	,, ,,	Sensitive 6 hours
,, 2	,,	Numerous	·25	,, ,,
,, 3	,,	,,	·30	Sensitive 3 to 4 hours
,, 4	,,	,,	·25	,, ,,

of serum, which is about the maximum dose a mouse can tolerate. The resistant strain from a mouse and a normal strain from a guineapig were both tested *in vitro* against normal human serum, and little if any difference could be seen in their behaviour. A dose of 10 million trypanosomes resistant to human serum in mice was injected into one European and 5 native volunteers. The results were again completely negative.

In a lengthy discussion which follows these interesting observations, Lester states that his original object was to ascertain whether *T. rhodesiense* occurs in Nigeria. From this work it appears that not only do strains having all the characteristics ascribed to *T. rhodesiense* occur, but that there is also a whole series of strains with characteristics intermediate between *T. rhodesiense* and *T. gambiense*. He then passes to a consideration of the question of the relationship between *T. gambiense*, *T. rhodesiense* and the game trypanosome in the light of his findings.

It is impossible to do justice to this interesting discussion in the very limited space available here, and those interested should consult it in the original. *W. Y.*

Corson (J. F.). **The Resistance of *Trypanosoma rhodesiense* to Normal Human Blood-Serum in Relation to Cyclical-Passage through Tsetse Flies.**—*Jl. Trop. Med. & Hyg.* 1933. Dec. 1. Vol. 36. No. 23. pp. 365–367. [11 refs.]

An experiment was performed with the object of ascertaining whether a strain of *T. rhodesiense* after cyclical passage through *G. morsitans* was more resistant to the action of normal human serum, when tested *in vivo*, than after a series of mechanical passages.

In his introductory remarks Corson points out that it is now generally recognized that although *T. rhodesiense*, when first isolated from man, exhibits considerable resistance to the action of normal human serum, this resistance is largely lost after a series of mechanical transmissions through experimental animals. Little work has, as yet, been done on the influence of cyclical transmission on this quality. Adams found that cyclical transmission (*G. palpalis*) caused diminished resistance, whereas Lester observed that experimentally produced serum fastness in *T. brucei* was transmitted by *G. tachinoides*.

In a table details are given of the effect of normal human serum on the infections in 32 rats inoculated directly from various human beings infected with *T. rhodesiense*. The dose of serum given varied from 0·5 cc. to 2·5 cc. [unfortunately the weight of the experimental rats is not given, but they are stated to be mostly half-grown ; this is obviously a matter of great importance in all work of this nature]. In no instance did the peripheral blood become negative. This shows that at the time of its removal from man *T. rhodesiense* is resistant to human serum.

A strain of *T. rhodesiense* was then obtained from an untreated case of sleeping sickness by inoculation of the blood into a guineapig. *G. morsitans* were infected from this guineapig. Two guineapigs and a rat were infected from the *G. morsitans*. From the rat the strain was carried by direct blood inoculation through 4 further rats and from the 5th passage a number of rats were inoculated in order to serve as a test of the sensitiveness of the strain to normal human serum. The guineapig strains were inoculated into other guineapigs, and on these clean *G. morsitans* were fed. These flies in turn infected a number of rats and also three other guineapigs from which rats were inoculated. These rats (infected either directly by the fly or inoculated from fly-infected guineapigs) served as a test of the sensitiveness to human serum of the strains which had passed twice through *G. morsitans*. The results of the tests are summarized in a table. Each rat was given 1 cc. of normal human serum. In the author's opinion it seems justifiable to conclude from this work that the trypanosomes in the rats infected by tsetse flies, and in those infected from the fly-infected guineapigs, were not more resistant to the action of normal human serum than were those in the rats of a series of mechanical transmissions. *W. Y.*

Steudel (Emil). Der Kampf gegen die Schlafkrankheit in Kamerun. [**Measures against Sleeping Sickness in Cameroon.**]—*Deut. Med. Woch.* 1933. Dec. 1. Vol. 59. No. 48. pp. 1798–1800.

This article is a criticism of the French sleeping sickness campaign in the Cameroons.

Steudel states that there can be no doubt that the distribution of sleeping sickness in the Cameroons has increased considerably since 1928. His main criticism appears to be that the French do not maintain

a sufficiently large staff of European doctors to deal adequately with the situation. JAMOT announced in 1930 that the French Government had voted 3,000,000 francs for sleeping sickness work in the Cameroons, and that this made it possible to increase the number of European doctors from 11 to 18, that of European assistants to 36 and that of native assistants to 400. If one remembers that there are in the bush about 130,000 cases of sleeping sickness, this means that there is only one doctor to 7,200 patients. Under the German régime there were 53 doctors, of whom 11 special sleeping sickness doctors and 13 military doctors were concerned in sleeping sickness work, whilst the number of sleeping sickness cases was only 4,000–6,000, *i.e.*, about 167–250 patients per doctor. Such a staff sufficed to produce good results. The French failure is due to the fact that the number of doctors available does not allow a proper search for patients and at the same time proper supervision of treatment. Steudel does not believe that JAMOT is correct, when he says that the accidents (specially blindness) following the use of atoxyl and tryparsamide were few; he thinks that many who suffered in this manner hid away in their huts lest worse should befall them from further treatment.

Other criticisms relate to JAMOT's views on lumbar puncture as an unnecessary guide to treatment, and to the fact that Bayer 205, or the French equivalent, is so little used in the Cameroons. *W. Y.*

RIOU & MOYNE. Un cas de trypanosomiase à évolution latente anormalement prolongée. [**A Case of Trypanosomiasis of Very Slow Development.**]—*Bull. Soc. Path. Exot.* 1933. Oct. 11. Vol. 26. No. 8. pp. 1090–1091.

Details are given regarding a case of sleeping sickness in which the evolution of the disease was remarkably slow.

The patient was a young girl, aged 12 years, belonging to the Mandiago tribe; she was born at Boudodry near Ziguinchor. When she was 4 years old she came to Dakar and has remained there ever since, not even leaving the immediate environments of the town. There was very little of interest in the history of the case: for a year she had exhibited enlargement of the cervical glands, and at times she appeared to be inattentive and to suffer from loss of memory, but these troubles were transient. When first seen by the authors she presented enlarged lymphatic glands, but no other signs or symptoms. Gland puncture revealed numerous trypanosomes.

W. Y.

LORÉ (A.) & MARTY (J.). De l'efficacité de la tryparsamide chez les trypanosomés en deuxième période. [**Efficacy of Tryparsamide in the Second Stage of Sleeping Sickness.**]—*Bull. Soc. Path. Exot.* 1933. July 12. Vol. 26. No. 7. pp. 959–965.

The authors discuss the question why, though in certain cases of human trypanosomiasis tryparsamide acts like a charm, in others it is a complete failure. The reason for the failures appears to lie in an acquired resistance; the patients who are rapidly benefited by tryparsamide are those who have never before been given the drug; those who are not benefited are the patients to whom tryparsamide was given when they were in the first stage.

For a number of years in the Cameroons the routine bush treatment has been atoxyl-tryparsamide in new cases and tryparsamide alone

in old cases. The great majority of cases so treated are in the first stage. When these cases enter the second stage of the disease tryparsamide no longer has any effect on their lesions ; notwithstanding repeated courses of treatment the issue is almost always fatal. Analysis of large numbers of cases at Ayos has shown the authors that the patients who passed into the second stage of the disease, after having received a course of tryparsamide, furnish the greatest proportion of deaths ; whilst, on the contrary, the patients in the nervous stage who have not before had tryparsamide are for the most part cured. It is remarked that even though they may have received other arsenicals, *e.g.*, atoxyl or novarsenobillon, they react quite well to tryparsamide. [This interesting and possibly important observation confirms that of Chesterman. Its explanation is not obvious because the reviewer and his colleagues have shown that atoxyl-resistance or salvarsan-resistance on the part of trypanosomes implies tryparsamide-resistance. A possible explanation may lie in the reputed diffusion of tryparsamide through the meningeal barrier, but the subject is one which obviously demands careful investigation on account of its great practical importance.] The authors add that resistance to tryparsamide seems only to be created when it is given before the changes in the spinal fluid have developed. Among 100 patients who died of trypanosomiasis 80 had been given tryparsamide before they passed into the second stage of the disease and only 16 had been given it for the first time when they were in the second stage ; of 100 patients who recovered only 16 were given tryparsamide before lumbar puncture showed the spinal fluid to be changed. Interesting details are given of a number of cases falling into each of the following groups : A—Those who had been given tryparsamide before they reached the second stage of the disease ; and B—Those who had not been given the drug before reaching the second stage.

The authors conclude from these observations that tryparsamide should be reserved for patients in the second stage of the disease.

W. Y.

Sicé (A.), Cousin (E.) & Rivoalen (P.). De l'utilisation de la tryparsamide appliquée au traitement de la trypanosomiase nerveuse. [**Utilization of Tryparsamide in Treatment of Nervous Trypanosomiasis.**]—*Bull. Soc. Path. Exot.* 1933. July 12. Vol. 26. No. 7. pp. 946–958. With 7 figs.

The authors have determined the rate of excretion of tryparsamide in the urine of a number of human beings who were given doses of the drug varying from 0·25 gm. to 3·0 gm. This was done with the object of ascertaining the quantity of the drug retained and really utilized by the organism after the administration of each of these doses. In another patient frequent estimations were made of the amount of arsenic in the blood in order to discover the length of sojourn of tryparsamide in the blood after a dose of 1·0 gm.

The various methods employed for the quantitative estimation of the drug in the urine and blood are described in detail ; three methods were used differing with the quantity of the drug present. This portion of the paper, which is of a chemical and rather technical nature, should be consulted in the original by those interested.

In their work on the elimination of the drug the authors confined their attention to the urine ; they did this not because they believe that this is the only channel by which arsenic is eliminated after

administration of tryparsamide, but because undoubtedly the great bulk of the drug is eliminated by this medium, and because, of all the excretions, the urine is most easily collected at regular intervals. In all cases the drug was given intravenously in 20 per cent. solution. Analyses were made in each case on the urine passed up to 3 hours after the injection, on the specimens passed between 3 and 6 hours, 6 and 9 hours and 9 to 12 hours, and subsequently on those passed between 12 and 24 hours, 24 and 36 hours, and 36 and 48 hours after injection.

The results of the quantitative analysis of these various specimens of urine from patients who had received respectively 0·25 gm., 0·5 gm., 1·0 gm., 2·0 gm., 2·5 gm. and 3·0 gm. of tryparsamide are shown graphically in a series of charts.

In the following table the results obtained after the injection of 0·25 gm. by tryparsamide are shown.

Time after injection	Vol. of urine cc.	Tryparsamide eliminated	Concentration per litre
3 hours	470	0·0749	0·1593
6 ,,	208	0·0266	0·1265
9 ,,	300	0·0098	0·0328
12 ,,	750	0·001	0·0012
12–24 ,,	1,800	0·0021	0·0011

From these figures it appears that during the first 24 hours 0·112 gm. of the drug was eliminated in the urine; consequently 0·138 gm. was retained. From this it is calculated that the "coefficient d'utilisation" is $\frac{0·138}{0·250} = 0·552$. It is noted that the drug continued to be eliminated during the following days, but that after the 7th day only traces which could not be measured were discovered.

Dose of tryparsamide given	Amount of tryparsamide found in urine during first 24 hours	Coefficient d'utilisation
0·25 gm.	0·112 gm.	$\frac{·138}{·250} = ·552$
0·50 gm.	0·117 gm.	$\frac{·383}{·500} = ·766$
1·00 gm.	0·313 gm.	$\frac{·687}{1·000} = ·687$
2·00 gm.	1·643 gm.	$\frac{·357}{2·000} = ·178$
2·50 gm.	2·093 gm.	$\frac{·407}{2·500} = ·162$
3·00 gm.	2·438 gm.	$\frac{·562}{3·000} = ·187$

In the same way the "coefficient d'utilisation" was calculated after each of the above-mentioned doses; the results obtained have been summarized by the reviewer in the above table.

In the single case in which the quantity of tryparsamide in the blood was determined at various intervals after a dose of 1·0 gm. of the drug the following figures were obtained.

Time after injection of tryparsamide	Quantity of tryparsamide in a litre of blood
30 mins.	0·02143 gm.
1 hour	0·01494 gm.
2 hours	0·00972 gm.
3 ,,	0·00705 gm.
5 ,,	0·00262 gm.
7 ,,	0·00240 gm.
24 ,,	0·00074 gm.
48 ,,	0·00070 gm.
72 ,,	0·00040 gm.

Analyses were not continued beyond 72 hours, because it was impossible to estimate such minute amounts with any degree of accuracy. Attention is drawn to the fact that the amount of tryparsamide in the blood after 2 hours (assuming the volume of this to be 5,000 cc.) was only 0·0486 gm., and that consequently no less than 0·9514 gm. had disappeared within this short period.

Summarizing these observations, it appears that whatever the dose of tryparsamide given—0·25 gm. to 3·0 gm.—a considerable proportion is eliminated in the urine within the first 3 hours; and the larger the dose the larger the quantity eliminated. After the first 24 hours the amount excreted becomes less and less, and after about the tenth day falls to such minute traces that they cannot be estimated quantitatively. Attention is drawn to the interesting fact that diuresis during the first 3 hours after administration of the drug accelerates its elimination in the urine.

The authors conclude that only a very small proportion of the dose of tryparsamide administered is retained and utilized by the organism in the effective combination which makes this drug so valuable in the therapy of the nervous stage of trypanosomiasis.

W. Y.

Barlovatz (A.); Chesterman (Clement C.). **Dosage of Tryparsamide in Treatment of Sleeping Sickness.** [Correspondence.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. Nov. 30. Vol. 27. No. 3. pp. 326–327; 327–329.

Barlovatz criticizes certain of the conclusions reached by Chesterman in his recent paper on the treatment of second-stage *T. gambiense* infections [this *Bulletin*, Vol. 29, p. 638–9]. He admits that, as Chesterman's figures for cures with high single doses are 50 per cent. as against 11·4 per cent. for small single doses, the correlation is striking. If, however, the cases be classified according to the total dosage given without regard to the size of the individual doses, then the tables show 22 per cent. of cures for a total dosage of less than

20 gm. as against 33 per cent. for a dosage of above 20 gm. Barlovatz hence considers that the total amount of drug injected is of importance. Furthermore, there appears to be some correlation between the severity of the nervous changes and the effect of treatment; Chesterman's cured patients had a mean cell count of 338, whereas those who died had 466. Chesterman's cases were mostly in very bad condition at the time of treatment and cannot be compared with the "secondary" cases usually encountered in routine sleeping sickness work. Before accepting his conclusions Barlovatz asks whether the cases to which Chesterman gave respectively large and small doses were selected quite at random, or whether they were chosen according to their supposed ability to stand high or low doses. This seems a fair question because it has long been the general practice to give small individual doses to bad cases.

Chesterman agrees that the total dosage should not be less than 20 gm., but he is at a loss to understand how Barlovatz deduces from his tables that 22 per cent. of cures were obtained with less than 20 gm. and 33 per cent. by over 20 gm. He himself quotes figures from the tables which make it difficult for him to accept the need for long courses in the type of case with which he had to deal; it is possible, however, that the majority of cases treated by field missions may do as well on prolonged medium, or small doses, especially if they come from newly prospected regions where there has been no possibility of the creation of resistant strains by inadequate treatment. He does not agree with Barlovatz's generalization that his cured cases had a lower spinal fluid cell count than had the fatal cases; and he re-asserts his previous conclusion that "The response of second-stage cases cannot be foreseen from the cell count of the cerebrospinal fluid." Chesterman agrees that in very advanced cases a preliminary small dose is justifiable. *W. Y.*

Barlovatz. Addendum à une communication sur les accidents dus au tryponarsyl. [**Accidents due to Tryponarsyl.**]—*Bull. Soc. Path. Exot.* 1933. July 12. Vol. 26. No. 7. pp. 929–930.

In continuation of his recent paper on this subject [this *Bulletin*, Vol. 30, p. 787], the author gives details of a chance observation which suggests that it is not safe to judge of the toxicity for the human subject of any sample of tryparsamide from its effect on small rodents.

A solution was made of a sample of tryponarsyl (series 1161) several years old, and some of it was injected into rats and the remainder into a number of cases of sleeping sickness. The rats received the following doses:—4 rats 1 gm. per kilo; 4 rats 2 gm. per kilo; 4 rats 3 gm. per kilo; and 4 rats 4 gm. per kilo of body weight. An hour later the same solution was injected intravenously, in an average dose of 0·04 gm. per kilo. (2 gm. per adult of 50 kilos.), into 30 sleeping sickness patients. All the patients quickly exhibited violent reactions, vomiting, rapid pulse, feebleness, sense of dissolution and prostration; these symptoms lasted some hours. Nobody died and the next day most of the patients were better, but some complained of headache. The rodents, on the contrary, exhibited no reaction whatsoever.

The author points out that many arsenical preparations, *e.g.*, salvarsan and its derivatives, are habitually first tested by trial on small rodents. The present observation indicates that toxicities of an arsenical for small rodents and for man are not necessarily parallel. *W. Y.*

VAN DEN BRANDEN (F.) & POTTIER (R.). Au sujet d'accidents dus à la tryparsamide et produits similaires. [**Accidents due to Tryparsamide and Similar Products.**]—*Bull. Soc. Path. Exot.* 1933. Oct. 11. Vol. 26. No. 8. pp. 1022–1026.

The authors suggest several reasons for the serious accidents (deaths and blindness) which BARLOVATZ had from time to time in the treatment of sleeping sickness with tryparsamide [this *Bulletin*, Vol. 30, p. 787].

BARLOVATZ encountered 22 instances of rapid death among the 1,700 patients treated; and in one day alone he had to deplore no less than 9 deaths. He records that the water used for dissolving the drug was heated to 70°C. and that the syringes had been rinsed out with carbolic acid. Van den Branden and Pottier in commenting on this pointed out that BARLOVATZ had not taken the precautions indicated years ago by POWERS, WEIGHTMAN, etc., the original manufacturers of the drug. Tryparsamide in the crystalline form is stable, but nevertheless is decomposed by chemical emanations and by high temperature and strong light. Solutions are less stable, and consequently must be freshly prepared: they must not be heated and not be exposed to chemicals and especially to phenol. The essential precautions are the use of sterile freshly distilled water as a solvent, the sterilization of the instruments, and strict asepsis.

In support of their contentions van den Branden and Pottier record a number of experiments performed on rabbits and rats. In these experiments, solutions of the drug were prepared in the five following ways:—

Method A. The correct method outlined above.
,, B. The drug was dissolved in distilled water at a temperature of 70°C. and then allowed to cool to 30°C. before injection.
,, C. As B, but injected at a temperature of 42°C.
,, D. The solution was boiled for 5 minutes and then cooled to 30°C. before injection.
,, E. The syringe was rinsed in 5 per cent. carbolized water and then, after being properly drained, was used for injecting the drug [the solution was presumably made in the orthodox manner].

Rabbits injected intravenously with a dose of 1·25 gm. per kilo.

Method A. 5 rabbits; no deaths; total gain in weight 515 gm.
,, B. 6 rabbits; 1 death on 5th day; total loss of weight 780 gm.
,, C. 5 rabbits; no deaths; total loss of weight 350 gm.
,, D. 6 rabbits; 1 death on 3rd day; total loss of weight 910 gm.
,, E. 6 rabbits; 1 death on 2nd day, 1 death on 6th day and 1 death on 8th day; total loss of weight of others 620 gm.

Rats injected subcutaneously with a dose of 3 gm. per kilo.

Method A. 3 rats; no deaths; 1 exhibited nervous symptoms.
,, B. 3 rats; 1 death; 2 exhibited nervous symptoms.
,, C. 3 rats; 1 death; 1 exhibited nervous symptoms.
,, D. 3 rats; 3 deaths on 4th, 5th and 6th days, respectively.
,, E. 3 rats; 2 deaths; 1 exhibited nervous symptoms.

Rats injected intravenously with a dose of 1·5 gm. per kilo.

Method A. 3 rats; no deaths; 1 exhibited nervous symptoms.
,, D. 3 rats; no deaths; 2 exhibited nervous symptoms.
,, E. 3 rats; no deaths; 2 exhibited nervous symptoms.

From these experiments it is concluded that heating the solution to 70°C., or boiling it, or rinsing the syringe with carbolic acid, increases the toxicity of the drug. [The authors may be right, but their data are not entirely convincing. In the reviewer's opinion they have hardly made sufficient allowance for the well-known variations in tolerance exhibited by individual animals of the same species.]

W. Y.

DE MARQUEISSAC (H.). Emploi de la médication mixte conjuguée : 205 Bayer-309 Fourneau + tryparsamide dans le traitement des réinfestations sanguines ou des échecs cliniques constatés chez les malades atteints de trypanosomiase à virus gambiense. [**Mixed Treatment of Bayer 205-Tryparsamide in Blood Reinfestations or Relapses** (*gambiense*).]—*Bull. Soc. Path. Exot.* 1933. Oct. 11. Vol. 26. No. 8. pp. 1051–1060.

This paper records the results of treating a large group of sleeping sickness patients in Togoland with a combination of Bayer 205 and tryparsamide. The considerations which induced the author to undertake this work were firstly that a certain proportion of cases were not sterilized by arsenicals alone, and consequently constituted a reservoir of the virus from which Glossina and other cases became infected; and secondly that the reviewer and his colleagues had shown that "arsenic-resistance" of trypanosomes is transmitted unimpaired through Glossina, and that this fact constituted a serious criticism of the French method of prophylaxis by wholesale atoxylization.

Dr. Marqueissac states that he did not attempt to use Bayer 205 (Fourneau 309) before any other treatment because of its cost, although he regards this as the ideal procedure. During the last 15 months he has, however, treated all cases in which arsenicals had proved impotent in the following manner:—The duration of the course of treatment was 12 weeks. During the first 4 weeks a weekly intravenous injection of Bayer 205 was given, the doses being 0·75 gm., 0·85 gm., 1·0 gm. and 1·5 gm. During the next 8 weeks a weekly subcutaneous injection of tryparsamide in the dose of 2·5 cgm. per kilo of body weight.

On Jan. 1, 1933, there were 8,073 cases of trypanosomiasis in the Pagouda sector of Togoland and of these 5,675 (70 per cent.) had been diagnosed since Jan. 1, 1931. The re-examination of 6,800 old cases diagnosed between 3 months and 4 years previously showed 409 (6 per cent.) to be still infected, notwithstanding previous treatment, and 230 of these were given a mixed treatment of Bayer 205 and tryparsamide. This method of treatment was inaugurated in March, 1932; in April, 1933—1 to 4 months after cessation of treatment—the blood of 167 was re-examined, and 156 (91 per cent.) were found to be free from infection. The previous treatment administered to these 167 cases was as follows:—

63 (37 per cent.) had been given one or several courses of tryparsamide.
46 (26 per cent.) had been given one or several courses of atoxyl.

49 (30 per cent.) had been given one or several courses of tryparsamide and trypoxyl.
9 (3 per cent.) had been given one or several courses of orsanine.

It is noted that of the whole 230 patients treated by this method during the last 15 months, only 6 had died.

Clinical relapses.—In certain patients the disease appears to progress towards incurability, notwithstanding all sorts of arsenical treatment; in fact arsenic seems merely to accelerate its progress. Since November, 1931, the author has used at the Pagouda dispensary and in the 19 centres for treatment in the sector, a mixed (synergic) treatment of Bayer and tryparsamide for all patients in the third stage, whether they be old cases or only recently discovered. The treatment consists in giving every 6 or 7 days an injection consisting of the two drugs. They are injected one immediately after the other without withdrawing the needle from the vein; the titre of the solutions used is 1 gm. of each drug in 5 cc. of distilled water. A course consists of 10 to 12 injections. The first dose given is 0·5 gm. of moranyl followed by 0·5 gm. of tryparsamide. If, after 3 or 4 injections, there is improvement, the amount of tryparsamide is slowly increased without altering that of moranyl, but the dose of tryparsamide never attains to the maximum therapeutic dose of the drug. Only 13 of 341 bad cases treated by this method during a period of 15 months have died.

The only serious ill-effect noticed in the treatment of these cases was that 5 of them developed an exfoliative dermatitis which proved fatal in two patients.

The article closes with an interesting note on the subject of Bayer 205 and albuminuria. Trypanosomes were found in the blood of 33 cases at Pagouda between Nov. 1932 and Jan. 1933. None of these had previously received any treatment. The urine of all was examined before and after treatment; in 25 (75 per cent.) of the cases albumen was found varying in amount from a trace up to (in 9 cases) a quantity equal to 1 gm. In 20 of these 25 patients the albuminuria disappeared completely after the first doses of Bayer 205, and in the remaining 5 patients there was a pronounced decrease in the amount. *W. Y.*

BERNY (P.). Action des arsénobenzènes sur les trypanosomes. [**Action of Arsenobenzol on Trypanosomes.**]—*Bull. Soc. Path. Exot.* 1933. Nov. 8. Vol. 26. No. 9. pp. 1161–1162.

Observations on three patients are recorded, which, in the author's opinion, afford support to the contention of HECKENROTH and BLANCHARD (1913) that neosalvarsan, although sufficing to sterilize the peripheral blood, fails to clear the lymphatic glands of trypanosomes [this *Bulletin*, Vol. 2, p. 587].

Berny points out that although this observation of HECKENROTH and BLANCHARD has never been confirmed, the arsenobenzols have disappeared completely from the therapy of human trypanosomiasis. He himself has, however, been able fortuitously to note the same phenomenon in two cases of syphilis and one of yaws. The first patient was given a dose of 0·3 gm. of novarsenobenzol, and the second two doses of 0·3 gm. and 0·45 gm. respectively. Two days after the last dose it was discovered that the patients had enlarged cervical glands: puncture revealed numerous trypanosomes in both cases, whereas triple centrifugations of the blood gave negative results. The

third patient, who had a generalized yaws eruption, was given 0·06 gm. and 0·12 gm. of sulpharsenol ; in this case also numerous trypanosomes were found in the glands 48 hours later, but none in the blood. *W. Y.*

VAN HOOF (L.). Essai d'un nouveau dérivé antimoine organique, Dn 12, dans la trypanosomiase humaine. [**Trial of a New Antimonial Derivative, Dn 12, in Human Trypanosomiasis.**]—*Ann. Soc. Belge de Méd. Trop.* 1933. Oct. 30. Vol. 13. No. 3. pp. 345–366.

This paper records the results obtained with the preparation Dn 12 in the treatment of human trypanosomiasis. This substance, which is a pentavalent antimonial compound of oxyquinoline, is a product of the Union Chimique Belge, and has already been tested on experimental animals infected with various trypanosomes [this *Bulletin*, Vol. 30, p. 788]. It is an orange-yellow powder, easily soluble in water, and stable.

A 5 per cent. solution of the drug was made in sterile distilled water and it was given intravenously in doses of 0·25 gm. to 0·50 gm. In all, 26 cases were treated : 7 with little or no meningeal reaction, 3 with definite meningeal reaction, 2 very advanced cases, 8 patients who had been previously treated with other drugs without success, 1 patient who had a double infection of syphilis and trypanosomiasis and who was given neosalvarsan as well as Dn 12, and finally 5 cases who had been found to have arseno-resistant infections. Detailed protocols of all these patients are given. The general plan of treatment appeared to be the administration of 0·5 gm. twice weekly until the patient had received a total amount of 5·0 to 10·0 gm. Many patients, however, were unable to tolerate such large amounts and, consequently, the individual dose had to be reduced to 0·25 gm. In a number of cases the larger dose provoked a crisis ranging from premonitory salivation, nausea and vomiting to short syncope or even to an attack which may resemble in all respects a definite anaphylactic crisis. In one patient who had already received a number of weekly doses of 0·25 gm. a similar dose was unexpectedly followed by a crisis of extreme gravity. Some minutes after the injection the patient had a sudden syncope, with vomiting, and this was followed by a period of shock which lasted more than four hours ; there was mydriasis, and subsequently myosis and blepharospasm, thready pulse, stertorous respirations with periods of apnoea, conjunctival injection, deviation of the eyes and relaxation of the sphincters. The author remarks that these shocks were so grave that he would have been unable to continue his investigations had he not found that preliminary treatment of the patient with sodium hyposulphite greatly reduced the tendency of the antimonial to produce shock. The hyposulphite (2 gm. in water) was either given orally two hours before the injection of Dn 12, or it was injected intravenously (0·5 gm.) immediately before the antimonial. It is noted, however that the efficacy of the hyposulphite seemed to decrease after a time and the author recalls that he has observed towards the end of a series of injections of Dn 12 unpleasant symptoms in patients notwithstanding the previous administration of sodium hyposulphite.

Even in the absence of immediate shock the drug may produce poisonous symptoms as the result of accumulation. These are headache, buzzing in the ears, various neuralgias and myalgias, loss of appetite, emaciation, anaemia, insomnia, and psychical excitation.

The most characteristic lesion is, however, antimonial dermatitis, which was seen in 4 cases.

The drug was found to exhibit a definite trypanocidal action ; it not only sufficed to sterilize the peripheral circulation, but in certain cases exercised a favourable influence on the cerebrospinal fluid. In certain cases, however, the drug was not only without action, but actually seemed to aggravate the condition. In an endeavour to explain these diverse results van Hoof points out that 17 of the cases were drawn from an endemic zone situated to the east of Léopoldville. The inhabitants of this area have, for a variety of reasons, only received insufficient treatment during the last 20 years and it is quite possible that during this period drug-resistant strains have gradually developed and are now being transmitted by Glossina. *W. Y.*

v. Issekutz (B.). Beiträge zur Wirkung des Germanins. Mitteilung I & II. [**On the Action of Germanin.**]—*Arch. f. Experim. Path. u. Pharm.* 1933. Nov. 24. Vol. 173. No. 4–6. pp. 479–498. With 5 figs. [14 refs.] ; pp. 499–507.

The experiments described in these papers were devised with the object of throwing light on the mechanism of the action of Bayer 205.

i. A technique was first developed whereby it was possible to measure the consumption of oxygen *in vitro* by a stated number (100 millions) of trypanosomes. The nutrient medium used was a modification of that introduced by the reviewer and his colleagues (1929). These authors had shown that provided the concentration of trypanosomes did not exceed about 2,000 per cmm., they could be kept alive *in vitro* at 37°C. on a medium consisting of equal parts of deactivated serum and Ringer-glucose solution for at least 24 hours. If, however, the concentration of parasites greatly exceeded this, then the trypanosomes died from want of glucose. Issekutz surmounted this difficulty at first by dialysis, but later by the simple expedient of adding his nutrient medium to tubes containing a little agar in which was incorporated 0·5 to 1·0 per cent. glucose : the sugar slowly diffused into the medium thus replacing what was removed by the trypanosomes. By means of a manometer it was possible to estimate the consumption of oxygen by certain known numbers of trypanosomes—the CO_2 was absorbed by filter paper moistened with 5 per cent. KOH.

Experiments performed with the aid of this technique showed that although neosalvarsan and trypaflavin greatly reduced the oxygen consumption of the trypanosomes and, in fact, actually destroyed the trypanosomes, " Bayer 205 " failed to do either. A series of normal rabbits were then injected with 50 mgm. per kilo. of neosalvarsan, with 100 mgm. of atoxyl and with 100 mgm. of " Bayer 205 " respectively. Blood was removed at intervals, and the effect of the various specimens of serum obtained on the oxygen consumption of trypanosomes *in vitro* ascertained. It was found that the serum of the rabbits which had received neosalvarsan or atoxyl were trypanocidal up to 24 hours after injection, but that the serum of the Germanin animal was without action.

Further observations made on infected rats showed that no matter what the degree of infection was at the time of administration of " Bayer 205," the drug exerted no obvious effect on the number of trypanosomes for at least 12 hours, and that it was not until the 16th to the 22nd hour that there was a great decrease in the number of

parasites. If infected rats were bled 6 to 9 hours after treatment with Germanin, the trypanosomes were found to exhibit their usual activity, but their capacity to consume oxygen and sugar was greatly decreased. Although such trypanosomes could be maintained alive *in vitro* at room temperature for 24 hours, *i.e.*, longer than they would have lived *in vivo*, yet, if the *in vitro* temperature were raised to 37°C., the parasites died as quickly as they would have done in the vertebrate host itself. From these experiments, the author concludes that there exists in the blood of an infected animal after treatment with "Bayer 205," a trypanocidal substance which is capable of acting only at body temperature.

Issekutz then performed a series of experiments in which infected rats treated with "Bayer 205" were killed at various times before and after the disappearance of the trypanosomes, and the trypanocidal power of the serum examined *in vitro* at 37°C. From these experiments he concludes that trypanocidal substances are not present in the blood up to the time of disappearance of the trypanosomes, but immediately after this event they begin to appear and as time goes on rapidly increase in amount. In the author's view a possible explanation of this phenomenon is that at first the trypanocidal substance is formed in such small amounts that it is all absorbed by the trypanosomes and so none is free in the serum, but after all the parasites are killed the trypanocidal substance continues to be produced and accumulates in the serum. It cannot be denied, however, that this hypothesis could only hold if it is found that "Bayer 205" is active after the entire reticulo-endothelial system is blocked, because it is only in this way that the production of immune bodies could be prevented. [Before Issekutz's hypothesis could be accepted it would certainly be necessary to exclude what appears to the reviewer to be the simplest explanation of the phenomenon, viz., that it was due to antibody formation.]

ii. A number of experiments were performed in which heavily infected rats were killed by bleeding at various intervals (4–9 hours) after treatment with Germanin (20–30 mgm. per 100 gm. of body weight). The trypanosomes were separated by centrifugation from the plasma, and then by the aid of Lang's colorimetric method (1931) the amount of "Bayer 205" present in the trypanosomes and plasma respectively was ascertained. The parasites were found to contain only 5–10·5 mgm. per cent. of the drug as compared with 24–42 mgm. per cent. in the serum. It is pointed out that 150 mgm. of trypanosomes did not contain sufficient drug to cure a lightly infected mouse. The oxygen consumption of these drug-laden trypanosomes *in vitro* was not decreased. Inoculation of such trypanosomes obtained from rats 9 hours after treatment was still infective for healthy animals, although the duration of the disease was prolonged. *W. Y.*

REINER (L.) & CHAO (S. S.). **Some Observations on Trypano Agglutinins and Lysins and their Production with Killed Trypanosomes.**—*Amer. Jl. Trop. Med.* 1933. Sept. Vol. 13. No. 5. pp. 525–534. [26 refs.]

Attempts were made to immunize rats against *Trypanosoma equiperdum* by means of vaccines consisting of dead trypanosomes.

In their early experiments the authors endeavoured to immunize rats and rabbits with trypanosomes killed by heat or by formaldehyde, but neither method proved successful. Finally, it was found that parabenzoquinone will kill trypanosomes in a fairly high dilution, but

does not destroy their morphology as do most of the other substances tested.

Preparation of the vaccines and immunization.—A $\frac{1}{50}$ molecular solution of quinone was prepared in physiological saline, and $\frac{1}{10}$ cc. of this solution was then added to 2·9 cc. of an emulsion of *T. equiperdum* in physiological saline and the mixture kept at room temperature for 30–120 minutes. As soon as microscopical examination of the suspension failed to reveal any evidence of motility among the trypanosomes, the emulsion containing about 100 million trypanosomes was injected into a rat. Eleven such injections were given within 14 days; and six to ten days after the last the rats were either bled to death, if it was desired to examine the agglutinating capacity of the serum, or they were inoculated with living trypanosomes if their resistance was to be tested.

For the determination of the agglutinating and lytic power of the immune serum, a suspension of living *T. equiperdum* in rat serum, inactivated at 56°C., was used, and to this was added varying quantities of immune serum. If no complement was added and the serum to be tested was inactivated, agglutination only occurred and no lysis. Fresh rat immune serum, or inactivated rat immune serum mixed with complement, also caused lysis of the trypanosomes if kept at 37°C. for 20 minutes. The results of four agglutination experiments are given in a table, from which it is seen that the agglutination titre was in one case 16, in two cases 32, and in one case 64. Readings were taken after 15 mins. at 37°C. Further experiments showed that there was a parallelism between the agglutinating and lytic powers of the sera, which, in the authors' view, suggests the identity of sensitizing and agglutinating antibodies.

The immune sera prepared in this way all showed a strict strain specificity without group reaction, *e.g.*, the strain of *T. equiperdum* maintained in rats behaved differently from the same strain passaged through guineapigs.

The results of one of the experiments, to test the acquired immunity of some of the immunized rats by injecting them with living *T. equiperdum*, are summarized in a table. It was found that the immunized rats always survived longer than the normal rats, but absolute immunity against experimental infection with 100,000 to 300,000 trypanosomes was only obtained in a small percentage of cases.

W. Y.

Schilling (Claus), with Schreck (H.), Neumann (H.) & Kunert (H.). Immunisierung gegen Trypanosomenkrankheiten. [**Immunization against Trypanosomal Diseases.**]—*Deut. Med. Woch.* 1933. Oct. 20. Vol. 59. No. 42. pp. 1603–1604; and *Bull. Soc. Path. Exot.* 1933. Oct. 11. Vol. 26. No. 8. pp. 1004–1008.

As the result of his reflections on the reason for the remarkable tolerance exhibited by the African antelope and other game animals to trypanosomes which are highly pathogenic for domesticated animals, Schilling puts forward the hypothesis that it is due to an immunity acquired shortly after birth, and that this immunity throughout life is constantly reinforced by bites of infected tsetse. In order to put this hypothesis to the test he performed a number of preliminary experiments.

The earlier experiments, which were conducted in 1913–1914 on calves and *T. brucei*, are not entirely satisfactory, as the strain was not

very virulent for cattle. The later experiments were conducted in Berlin between 1930 and 1932. In these, foals and the highly virulent *T. congolense* were used.

A foal born on 16 Oct., 1930, was given 8 days later a subcutaneous injection of dried *T. congolense* antigen. On the 18th and 23rd days after the vaccination the animal was bitten by *G. morsitans* (bred in the Robert Koch Institute) infected with *T. congolense*. This was followed by a period of irregular fever, which lasted up to the 67th day ; thereafter, except for occasional rises, the temperature remained normal, the last febrile disturbance being on 2nd May, 1932. Trypanosomes were last seen on 23rd Feb., 1932. The weight had increased from 40 kgm. to 400 kgm. on 20th Sept., 1932, and the animal was healthy and active. On 20th Sept., 1932, its blood was injected into mice with negative results. On 22nd Sept., 1932 (23 months after vaccination), infected tsetse were again fed on it with the result that there was an energetic reaction—fever, loss of weight, and trypanosomes in the blood. Three further infections by means of tsetse produced but slight reactions.

A second foal was infected by tsetse and then treated by a half curative dose of antimosan, and subsequently subjected to the bites of infected tsetse. This animal behaved very much as the previous one. Schilling intends to apply his methods in Tanganyika. *W. Y.*

Krijgsman (B. J.). Biologische Untersuchungen ueber das System : Wirtstier-Parasit. III. Teil : Das Verhalten der Blutproteine und IV. Teil : Das Verhalten des Blutzuckers während der Entwicklung von *Trypanosoma evansi* in der Ratte. [**Biological Investigations on the System : Host-parasite. III. The Behaviour of the Blood Proteins, and IV, the Behaviour of the Blood Sugar during the Development of** *T. evansi* **in the Rat.**]—*Ztschr. f. Parasitenk.* 1933. Sept. 6. Vol. 6. No. 1. pp. 1–22. With 5 text figs. [63 refs.]

Experiments were performed with the object of ascertaining whether any changes occurred in the various serum proteins or in the blood sugar titre during the course of *T. evansi* infections in rats.

The author remarks that the system " trypanosome-mouse " in which the progressive inhibition of division is absent is less complicated than the system " trypanosome-rat " in which three factors, which inhibit development of the parasite, appear. Since, however, the technique for chemical analysis of the blood necessitates more blood than can be obtained from the mouse he was compelled to use the " trypanosome-rat " system. Estimations of the protein fractions required about 1·5 cc. of blood, and hence it was not possible to make a series of investigations on one animal ; accordingly, a number of rats were infected with similar quantities of the parasite at the same time, and every six hours afterwards an animal was sacrificed and its blood collected. In this way it was possible to reconstruct curves of the trypanosome development and concentration of blood proteins. The technique employed for estimating the protein fractions was that of von Rusznyak (1923) ; it consisted essentially in precipitating the various proteins with different concentrations of ammonium sulphate solution and estimating the cloudiness produced by a nephelometric method (Pulfrich's photometer). As the technique for determining the blood sugar titre (a modification of Folin's with the aid of a Pulfrich's photometer) required only 25 cmm. of blood, it was possible to follow the

blood changes throughout the course of the infection in a single animal.

In the work on the serum proteins 33 rats were killed in various stages of the infection. The results of the analyses, which are set forth in a table, show that the blood proteins remain unchanged throughout the course of the disease, whether its development be rhythmically progressive, slowly progressive, or intermittent. There was no definite variation either in the content of total blood protein or in that of any of the protein fractions.

Similarly blood sugar estimations made in rats in which the infection was—(i) rhythmically progressive, (ii) slowly progressive, or (iii) intermittent, failed to reveal any definite changes apart from the well-known pre-agonal hypoglycaemia. Experiments were then conducted to ascertain whether altering the blood sugar content either in the positive direction by the administration of adrenalin and glucose, or in the negative direction by insulin had an influence on the infection. From the first of these experiments it is concluded : that the sugar content of normal blood is in excess of that required for the metabolism of trypanosomes, that raising the sugar content does not accelerate the development of the parasites, and that adrenalin itself has no direct action on the trypanosome development ; and from the second—that there is always in the blood an amount of sugar in excess of that required by the trypanosomes and that insulin has no action on the development of the parasites. *W. Y.*

Topacio (Teodulo). **A Simple Technic for isolating Single Trypanosomes.**—*Philippine Jl. Sci.* 1933. Aug. Vol. 51. No. 4. pp. 631–635. With 4 plates.

The technique consists essentially in making a stock suspension of trypanosomes in 30 per cent. plasma of such strength that when a small drop is examined under the low power of the microscope, it is found to contain 3 or 4 organisms. From this stock suspension a series of minute drops are transferred by means of a capillary glass rod with a rounded end to a strip of sterile cellophane paper mounted on a glass slide by means of sterile serum. About 10 separate drops are deposited on the cellophane paper 8 mm. apart. The drops are then examined under the low power of the microscope. Immediately a drop is recognized to contain only a single organism, a little more 30 per cent. plasma is superimposed, and the observer then passes to the examination of the other drops. The author remarks that it is often possible by this simple procedure to obtain 3 or more drops containing single organisms. Each drop with a single organism is removed from the slide by cutting a small square through the cellophane paper mount around the drop. The article is clearly illustrated by a number of plates. *W. Y.*

Corson (J. F.). **A Modification of Lloyd and Johnson's Method of Proboscis and Gland Dissection in Tsetse Flies.**—*Ann. Trop. Med. & Parasit.* 1933. Oct. 21. Vol. 27. No. 3. p. 481.

The author recommends the following technique for removing the salivary glands from Glossina :—

" Instead of first removing the head with the glands from the thorax, the head and thorax preparation is laid on its back in normal saline, the left needle slightly pierces the thorax about between the third pair of legs to hold the specimen, while the right needle is laid horizontally across

the base of the proboscis. By gentle pulling, the proboscis is pulled off the head and draws the glands out with it. It is easy to do and is successful with freshly killed flies." *W. Y.*

JACKSON (C. H. N.). **On the True Density of Tsetse Flies.**—*Jl. Animal Ecology*. 1933. Nov. Vol. 2. No. 2. pp. 204–209.

——. **On a Method of marking Tsetse Flies.**—*Ibid.* pp. 289–290.

Our present knowledge of the numbers of wild tsetse flies is based almost entirely on the fly-count ; but this is affected not only by the number of the flies, but also by their activity at the time when the count is taken. In spite of their manifest imperfections, far-reaching conclusions have been drawn from fly-counts. The author feels that some entirely new technique is necessary.

Jackson points out that, if one could find an area inhabited by Glossina and completely surrounded by some type of vegetation which that insect does not pass, it should be possible to arrive at an absolute estimate of the total number of flies. This he would do by catching, marking and liberating a certain number. After an interval, a considerable number of flies would be recaught, the ratio of the marked to the unmarked giving a measure of the population assuming that no deaths or births had occurred. After preliminary work, this method was applied to an area of about $2\frac{1}{2}$ square miles which was inhabited by *G. morsitans* and almost completely surrounded by impassable barriers. Flies were caught and marked on five successive days, and on the three following days a large number were recaught. Assuming that the mean duration of life is one month, *i.e.*, that 3 per cent. of flies die daily, the conclusion was arrived at that the area contained a population of a little under 2,000 male *morsitans*. [It is known that marked flies are occasionally recaptured after long intervals, so that it is clear that the method does not generally do them serious harm. But we believe that nobody has ever investigated the death-rate in cages among marked and unmarked flies ; it may well be that there is a considerable death-rate, particularly in the day or two following the manipulation. If it could be shown that marking causes no increase in death-rate, then the author's investigations could most profitably be extended, for the gradual disappearance of the marked flies would be a measure of the deaths among the unmarked.] The author also considers the possibility of applying some similar method to an area which is not isolated, and which receives and loses flies continually. He suggests a theoretical method of studying such a problem, but he has not yet been able to obtain results which he can accept.

The second paper describes ingenious methods of marking Glossina with oil paints. They can be marked on a two-colour system, which enables each day's batch to be distinguished over a long period. There are, moreover, individual marks which can be applied to a particular fly even if it is recaptured on more than one occasion. *P. A. Buxton.*

NASH (T. A. M.). **A Statistical Analysis of the Climatic Factors influencing the Density of Tsetse Flies,** *Glossina morsitans* **Westw.**—*Jl. Animal Ecology*. 1933. Nov. Vol. 2. No. 2. pp. 197–203. With 2 plates.

The author has developed a standard technique for counting *Glossina morsitans* on fly-rounds. He has applied this at regular intervals for

4½ years in a particular area in Tanganyika. He has also meteorological data for the same period, and a preliminary graphical examination has suggested that evaporation has more effect on numbers of fly than other meteorological factors. He now proceeds to examine the same question statistically.

In the present paper, the numerical data are examined by correlation coefficients which are used with exemplary caution. The period over which the data were collected included a time of unusual inundation, and it seems that this reduced the fly community so much that it required about 18 months to make a complete recovery. The author, therefore, presents correlation coefficients for the whole period under study (35–40 months in the case of most climatic elements) and also for the last 22 months, a period which was not affected by the flood. His general conclusions are that the negative correlation between fly and evaporation (or saturation deficiency) is high and significant: that is to say, the drier the air, the lower the fly-count. There is, as might be expected, a considerable positive correlation with rainfall, for the rainfall produces a higher humidity, that is to say, a lower evaporation. But there is, unexpectedly, no significant correlation with temperature. It is also extremely interesting that there is a high and significant correlation between evaporation, saturation deficiency and rainfall and the fly-count of the succeeding month. This shows that the fly-count does give a measure of the number of flies and not only of their activity at the time when the count is made. It has, of course, always been assumed that this was the case, but we do not think that it has ever been proved in so conclusive a manner. Needless to say, it remains probable, indeed almost certain, that the fly-count is also influenced by the activity of the insects, so that it is not entirely a measure of numbers.

The author's approach to this difficult problem is new and cautious. It would surely be advantageous if similar work could be carried forward with more complete meteorological data. *P. A. Buxton.*

Zuccarini (J. A.) & Oyarzabal (J. D.). Sur l'existence du *Trypanosoma cruzi* à Cordoba (R.A.). [*T. cruzi* **at Cordoba (Argentine).**]—*Folia Biol.* Buenos Aires. 1933. Oct.–Nov.–Dec. Nos. 31–32–33. p. 151. [Spanish version p. 146.]

In May last, whilst examining systematically for malaria parasites the blood of the inhabitants of La Canada in the south-west of Cordoba, the authors came across a case of infection with *Trypanosoma cruzi*, a child born in the district 8 months previously. Regular examinations of the blood up to the beginning of September always revealed small numbers of trypanosomes, and subinoculations of the blood into susceptible animals were positive. Apart from micropolyadenitis there was no symptom. The electrocardiogram was normal. *W. Y.*

Geoghegan (Arnoldo J.). Dos nuevos casos de tripanosomosis humana americana en la prov. de Catamarca. [**Two More Cases of American Trypanosomiasis in Catamarca Province, Argentine.**]—*Folia Biol.* Buenos Aires. 1933. Oct.–Nov.–Dec. Nos. 31–32–33. pp. 147–148.

Two fresh cases here recorded brings the total seen by the author in Catamarca to five, four of them coming from the capital. Both these

now detailed were young children; one was 3½ months old, the other 8 months.

The first showed *Tr. cruzi* in the blood, but inoculation (a small quantity only, obtained by cupping, was available) into white rats was negative. Clinically the signs were a yellowish tinge on the face, some exophthalmos, enlargement of the submaxillary and cervical glands, distended abdomen, enlarged liver and spleen, oedema of face and ankles. The mother stated that the illness had begun two to three months before with fever, irritability and convulsions [? twitching] during sleep. No other members of the family showed trypanosomes in their blood. The patient could not be further observed as the family moved from the district. It is stated that the Triatoma was common in tree trunks, especially that of the black carob bean (algarroba negro), but very exceptionally they were seen in the houses.

The second patient had trypanosomes in the blood and inoculation into a white rat proved positive. The child was slightly febrile (38°C.) and the attack had started 20 days previously with high evening temperature; the skin was yellowish, straw-coloured, and there was slight facial oedema, irritability and convulsions during sleep. When examined subsequently [how much later is not stated] the child appeared to be well and no trypanosomes could be seen in the peripheral blood. *H. H. S.*

Dunn (Lawrence H.). **A Natural Infection of *Trypanosoma cruzi* Chagas found in *Rhodnius pallescens* Barber in Panama.**—*Amer. Jl. Trop. Med.* 1933. Sept. Vol. 13. No. 5. pp. 471–473.

A recently described reduviid bug, *Rhodnius pallescens*, collected in a hut in a small village, Aguas Buenas, near Panama city, was found to be infected with *Trypanosoma cruzi*. Guineapigs on which the bugs were fed became infected, but so far no infection has yet been found in the members of the family occupying the hut, viz., 3 adults and 2 children. The author notes that the first case of Chagas' disease recognized in Panama was in a child living in a hut near Aguas Buenas, and a few months later, in 1931, three other children in the same village were found to be infected. *W. Y.*

Stein (L.). Chemotherapeutische Versuche bei der Chagaskrankheit (*Schizotrypanum cruzi*). [**Chemotherapeutic Experiments in Chagas Disease.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1933. Vol. 80. No. 1/2. pp. 1–15. [24 refs.]

Experiments were undertaken to ascertain whether certain compounds of bismuth and atebrin had any influence on *T. cruzi* infections in mice.

After giving a summary of previous attempts to find a cure for this infection, the author passes to a detailed account of his own work. The compounds used were:—R 141 (bismutho-αα- dithiopyridin-γ-sodium carbonate); R 1220 (another compound prepared by Rothmann somewhat resembling R 141); Bismutho-yatren A (bismuthyl-7iodo-8oxychinolin-5sodium sulphate); Bi 5 (Pallicid) *i.e.*, tri-bismuthyltartrate; Bi-diasporal 360 (a radio active bismuth compound); and atebrin.

None of these compounds had any effect on the fully developed infection, but all the bismuth compounds except R 1220 prevented the

development of the infection when they were injected at the same time as the virus. Atebrin alone had no effect, but when given in combination with R 1220 produced a prolongation of the infection. *W. Y.*

Maclean (G.). **Memorandum on Sleeping Sickness Measures.**—Tanganyika Territory Medical Department. 6 pp. 1933. Dar Es Salaam: Govt. Printer.

——. **Sleeping Sickness Notes.**—Tanganyika Territory Medical Department. 7 pp. 1933. Dar Es Salaam: Govt. Printer.

These articles, which deal with sleeping sickness problems as met with in Tanganyika, are of a semi-popular nature and require no special notice. *W. Y.*

Advier (M.) & Schennberg (P.). Un cas de maladie du sommeil contractée par un Européen aux environs de Dakar.—*Bull. Soc. Path. Exot.* 1933. June 14. Vol. 26. No. 6. pp. 869–871.

Biologie Médicale. 1933. Supplement to No. 4. 56 pp.—Documentation clinique et expérimentale sur l'action trypanocide de l'Orsanine Sodique (1926–1932).

REVIEWS AND NOTICES.

CELLI (Angelo) [the late]. Edited and Enlarged by Anna CELLI-FRAENTZEL. **The History of Malaria in the Roman Campagna from Ancient Times.** With a Preface by Sir Aldo CASTELLANI, K.C.M.G. (Hon.), D.S.C., M.D., F.R.C.P.—pp. viii + 226. With 1 folding map. 1933. London: John Bale, Sons & Danielsson, Ltd., 83–91 Great Titchfield Street, W. 1. [10s. 6d.]

This is the story of the Campagna down the centuries, and of its rediscovery through the devotion of Angelo Celli as a land of promise for his countrymen. Professor Celli was engaged in writing a history of malaria in the Campagna at the time of his death; he had collected an immense amount of material for his subject and a debt of gratitude is due to Madame Celli who has arranged and edited it. The book is a literary museum of extracts and citations from Ovid, Strabo, Livy and Cato in classical times, from countless ecclesiastical and other documents in the middle ages, and from Shakespeare, Addison, Dickens and many others in modern times. Its main theses are, firstly, that the desolation of the Campagna was due neither to war nor to the rapacity of the great landowners, but to malaria, and, secondly, that prophylactic quinine is the magic weapon which has at last brought victory.

The Campagna has not always been malarious; the immense ruins of Etruscan cities testify to its healthiness in pre-Roman days, and during the early centuries of the Republic there was little malaria, but it became prevalent after the second Punic war, in about 200 B.C. It declined during the Empire, and, until the Sack of Rome by the Goths in 410 A.D., the villas of the Campagna maintained their splendour unimpaired. During the following centuries all attempts to colonize were ruined by malaria, and it was not until the Renaissance that the disease declined once more and the nobles of Rome built their palaces along the shores of Latium. This prosperity was destroyed by the Sack of Rome in 1527, and from that time until the end of the 19th Century the Campagna was a desert ruled by malaria.

When Italy became a united kingdom in 1870, Garibaldi believed that the papal régime was responsible for this desolation; the estates of the Church were confiscated, and from 1885 to 1890 vast drainage works were carried out by the State; but failure followed failure, all attempts to colonize were fruitless, and, in 1898 the work was abandoned. The situation was saved by Angelo Celli who discovered the road leading from the laboratory to the open country. He founded the Association for the Study of Malaria, and owing to its efforts the quinine laws were passed. Under these laws the State control of quinine was established, employers were held responsible for supplying it to their labourers, and free quinine was issued to the poor. In the 18th and 19th Centuries quinine was used only for the treatment of the sick, but, in recent years, it has been employed as a prophylactic, and, armed with it, the Italians are re-conquering the Campagna. Before an area is reclaimed a sanitary staff composed of 45 physicians assisted by trained nurses arrives, and, while the land is being drained, the health of the labourers is protected by quinine. As a result, the number of patients in the hospitals of Rome is lower than it has been for 20 centuries, and the coast of Latium, from Civitavecchia to Nettuno, has been transformed from a hotbed of malaria into a health resort. *W. Fletcher.*

ESSED (W. F. R.). **Over den Oorsprong der Syphilis. Een Kritisch-Historisch-Epidemiologische Studie tevens ontwerp eener nieuwe Theorie.** [The Source of Syphilis. A Critical Historical Epidemiological Study together with a New Theory.]—pp. vi.+328. With 3 figs. on 2 plates. 1933. Amsterdam: H. J. Paris.

Publications of recent years on tropical medicine have dealt with the question—*Is* yaws syphilis? In this book, however, an entirely new turn is given to the question by its transformation to—*Was* syphilis yaws? The epidemic of syphilis at the end of the 15th century, a highly contagious disease, spreading through country after country, has been responsible for much disputation on where the guilt of origin lay. In the author's opinion it was undoubtedly a "New Sickness" and he discusses in this closely reasoned, highly documented book the opinions of a great range of authorities. He thus introduces us to a wealth of historical information of a very interesting sort. We read in the first place how this new, deadly and decimating malady could be accounted for by the conjunction of Jupiter and Saturn in the sign of Scorpio. There arose then the two camps of disputants, the Scorpionists and the non-Scorpionists. Other fantastic explanations of the sickness, many of them based on the prevalent humoral theory, are also reviewed. The real subject matter of dispute, however, centres round the introduction into Europe of the disease from America after its discovery by Columbus. We are required to call ourselves Americanists or Antiquarians according as we uphold the doctrine of introduction of the disease to Europe by Spanish sailors and its infliction upon a virgin soil, or throw in our lot with the contestants for an exacerbation of an ancient, existing disease, well known to the Arabs, the Greeks and the Romans. The mummies of Egypt contribute their share to this side of the question. A variation in approach to the subject, which, however, is dismissed by the author as inconceivable, is that of BOERHAAVE, following SYDENHAM, who attributed the introduction of syphilis into the New World to the slave traffic from the African Gold Coast. The European epidemic of "syphilis," however, was at the end of the 15th century, whereas the first transport of slaves only took place in 1502.

We might linger at length on all sorts of curious information before relinquishing this historical disquisition. We might enter along with the author, into the merits of the names given to the New Sickness—the Spanish Disease, an allusion to the introduction by sailors from America, the *Morbus Gallicus* in agreement with the theory of its diffusion upon the disbandment of the army of Charles VIII of France in 1495, or the Italian disease which would represent its origin as essentially due to the war of Naples. In this war an army of mercenaries was engaged and was less intent upon soldiering than upon the opportunities for looting and much excess "*in baccho et venere*." We restrict ourselves, however, to one reference only, for its national interest. It is instructive to discover that, whereas at the present time the town of Edinburgh is agitating for parliamentary sanction to compulsory notification of syphilis, this sanction in a highly rigorous sense was already put into effect by the Scottish ruling authorities for the "New Disease" in the reign of James IV. All sufferers from the "Grandgor" were ordered to quit the town by a fixed date and betake themselves to Leith where they would find boats to convey them to the island, the Inch, on which they were to remain till well. Those who

failed to comply with this drastic quarantine regulation ran the risk of being branded on the cheek.

Up to the end of the first part of the book the author, although insistent on the conception of the disease being *new*, gives full weight to a consideration of the argument of the "Antiquarians" the protagonists for an *Altertumssyphilis*. At this point he presents the reader with his mode of escape from the alternative of being an Americanist or a non-Americanist by maintaining that the epidemic syphilis, called the Spanish Pox, the Bubas, was not syphilis as we know it at the present time. The title of the second part of the book gives the author's point of view—The New Sickness which was brought to Europe, Africa and Asia after the discovery of America was not syphilis but yaws. The first chapter of the second part treats of the symptom complex of yaws and then follows a succession of chapters on the *Morbus Gallicus*. In the 7th chapter we find those arguments on which the author's theory rests taken up *seriatim* to the number of forty-one. Naturally this chapter deals extensively in its medical section with the differential diagnosis between yaws and syphilis. In the next chapter, which relates to the length of time during which the malady remained in Europe, the conclusion is reached that it lasted for two centuries after being brought over by Columbus. Yaws was still present in England at the beginning of the 19th century. The very last among the author's conclusions, to which we shall presently refer, is that the conception of "endemic syphilis" is incorrect and a special chapter is devoted to this aspect of the question. In this chapter we find that the "so-called endemic syphilis received different names in different countries." There were the radesyge of Norway and Sweden, the sivvens of Scotland, the button scurvy of Ireland, the "syphilis" of Canada, the scherlievo of Italy, the frenga of Servia and the spyrokolon of Greece. All of these appear to have been yaws. Nor does this view come unsupported. We have, for example, this quotation from an article by a Dr. James Thomson from Jamaica in the *Edinburgh Medical Journal* of 1819—"I have by me the notes of an old practitioner of this island who went home to a part of Scotland where the sibbens was prevalent. His remarks are made without any allusion to theory and they tend to confirm *the identity of yaws and sibbens* in many particulars. . . ." Even in the 20th century yaws makes at least one dramatic reappearance in Europe, for during the great war two American soldiers, diagnosed as suffering from impetigo contagiosa, had this diagnosis changed to yaws at the instance of a Brazilian doctor.

A review such as this can scarcely do justice to the contents of a work of this kind, nor have we gone in detail into the points of difference between yaws and syphilis. The author's conclusions, briefly expressed, are that syphilis has always been present in Europe. It was not syphilis but a new disease, introduced by the sailors of Columbus, which spread as an epidemic at the end of the 15th century and this disease was yaws. The new disease ultimately became confused with syphilis and the two were classed together as one and the same venereal disease. *W. F. Harvey.*

Rockefeller Foundation. **Annual Report 1932** [Mason (Max), President].—pp. viii+455. With 45 illustrations. New York: 49 West 49th Street.

In these difficult times, when the Governments, Universities and other Educational Institutions of nearly all countries find themselves

obliged to cut down expenses in any way that they can, scientific research is one of the first subjects to fall under the axe of retrenchment ; it is therefore even more than usually welcome to learn from this Report that the manifold activities of the Rockefeller Foundation, during the year 1932, show no signs of diminution. As usual, the principal items of expenditure were for the promotion of research work both in the laboratory and in the field, work and education in Public Health, and Fellowships and Grants in Aid : the great power for good, exercised by the Foundation, is much enhanced by the continuity of policy which it is able to maintain.

The Report is of considerable scientific interest and practical value ; there are sections on yellow fever, malaria, ankylostomiasis and other tropical diseases, on State and Local Health Services, on Public Health education and the training of nurses. Much information and many suggestive ideas can be gleaned from these summaries of the work done during the year.

Under yellow fever it is reported that it is evident, from the result of blood examinations, that widespread unrecognized epidemics have occurred in recent years in many parts of the interior and in the coastal areas of West Africa. In the section on malaria attention is drawn to the various local races of *Anopheles maculipennis*, the importance of which is now recognized. From the beginning of the work of the Rockefeller Sanitary Commission, in 1909, much attention was given to hookworm disease, and the Rockefeller Foundation carries on the work with the same vigour. In 1932 an epidemiological and bacteriological study was made of the common cold in an Arctic climate. It was found that, in a community of about 500 people in Spitzbergen, the incidence of the common cold is about one attack per person per year. An annual epidemic follows the arrival of the first ship in the summer ; this epidemic lasts for about six weeks, and a few second attacks occur. Soon afterwards colds practically disappear, and only four cases were reported in the last three months before the next shipping season.

Demonstrations in Public Health subjects were given in eight European countries ; field and laboratory research was continued, and much practical work was done. There was also much activity in this subject in North, Central and South America, in China, and other countries.

Large grants were made to various Institutions for the promotion of research in the fields of neurology and psychiatry.

The Report makes cheerful reading, and shows plainly how ably the large resources of the Rockefeller Foundation are administered by the Members and Executive Committees. *H. J. Walton.*

Shattuck (George Cheever) [M.D., Assistant Professor of Tropical Medicine, Harvard University Medical School], in Collaboration with Others. **The Peninsula of Yucatan. Medical, Biological, Meteorological and Sociological Studies.**—pp. xvii + 576. With frontispiece, 68 plates & 30 text figs. Carnegie Institution of Washington Publication No. 431. 1933. Washington.

The first, second and third Yucatan Medical Expeditions which were in the field in 1929–1931 and the results of which appear in this handsome volume were organized at the instigation of the Carnegie Institute of Washington by the Department of Tropical Medicine of Harvard University, of which Professor Shattuck is a distinguished member. Their object was to make a survey of disease in the State

of Yucatan which, together with historical evidence of disease in the Peninsula, might throw light on the collapse of the Mayan civilization.

The results of each Expedition are recorded separately, so that the information is scattered, but the chief results of the first two Expeditions are summed up in Chapter 21.

Regarding the Pre-Columbian period it is thought that dependence upon local supplies of impounded water in this arid area must have meant a heavy mortality from intestinal affections. Tuberculosis was probably absent. During the "period of the Conquest," 1502 to 1697, yellow fever and smallpox, imported from Africa, must have decimated the Mayas; malignant tertian malaria was probably imported about the same time. In the modern period there was a devastating outbreak of cholera in 1833. The results of the present survey make it evident that dysentery and similar infectious diseases of the intestinal tract are responsible for about one-third of the deaths in the State. The greatest health problem is the supply of safe drinking water at low cost. The second place in the causes of death is taken by malaria or respiratory diseases. Of increasing importance in the future will be leprosy and tuberculosis. Syphilis appears to be almost negligible in its incidence. Trachoma may become a health problem in the future. The chicle gatherers should be protected from chiclero ulcer, which in many cases is leishmanial.

The first two Expeditions took place in the winter or dry season. The third was in the summer, the rainy months, and was mainly for the purpose of studying the incidence of malaria and amoebic dysentery. In the malaria survey 2,353 patients were seen and 2,198 blood smears examined: only 48 or 2·2 per cent. were positive. The prevailing parasite was *P. vivax*. As the author observes, this is almost negligible for a tropical country where malaria is endemic. In spite of frequent searches anophelines, either adult or larval, were never found. The transmitter is believed to be *A. albimanus*.

Examinations for amoebae were made in 1,362 stools from 854 persons; 166 or 19·5 per cent. were infected with *E. histolytica*. Since not more than 1·5 examinations per person were made the true incidence is estimated at 40 per cent., an incidence which on the basis of findings elsewhere is believed to be near the average for tropical countries. Active amoebic dysentery was noted in 28 persons or 3·3 per cent.

J. C. Bequaert writes on the entomology of Yucatan. Extreme arid conditions during the dry season and scarcity of permanent superficial water account for the small number of blood suckers. C. C. Hoffmann has written on the Anopheles of Mexico [see this *Bulletin*, Vol. 29, p. 688]; 6 species are reported from the Yucatan peninsula. Though Yucatan used to be an endemic centre of yellow fever *Aëdes aegypti* does not occur anywhere in large numbers. The only really common domestic mosquito is *Culex quinquefasciatus*.

For reasons given it is thought that Dr. Lara's record of paragonimiasis in Yucatan [this *Bulletin*, Vol. 3, p. 287] is doubtful and should await confirmation. There is much else that is of interest in the volume, especially on the sociological and anthropological sides. The photographs are beyond praise. *A. G. B.*

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